

# DISEASES of the CHEST

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## Foreseeing and Forestalling Tuberculosis\*

### Introduction to Symposium

A. H. W. Caulfeild returned from the laboratories of Sir Almroth Wright in Britain and of Wassermann in Germany, in the spring of 1909, three years after the latter had announced his epoch-making test. At the instigation of the late Sir. Wm. Gage, the National Sanatorium Association had appointed Caulfeild to the staff of the Muskoka Hospital for Tuberculosis at Gravenhurst, Ontario, to organize and be chief of a Research Laboratory. He at once, along with other things, began carrying out the Tuberculo-complement-fixation with patients' sera—a fixation with a specific antigen, in contrast to the Wassermann—a fixation with a non-specific antigen. In a few months Caulfeild noticed an appreciable lack of correlation between the T.C.F. reaction and the clinical course of the cases. He then changed the principle of the test until an essentially different test was evolved.

On an evening early in 1910, Caulfeild came to the medical library of his associate and friend, the writer, to look through other medical journals. He had noted this particular reaction for the first time and desired to know if there was any mention of others having noted the same reaction. He found that it had been reported upon by two separate workers, namely by d'Este Emery in England and by Calmette in France. The latter called it the "Inhibiteur" Reaction; Caulfeild called his the "Inhibitive". For the best part of the next year Caulfeild worked on a monograph on this test, not knowing whether others were doing the same. When his paper was published in 1911 nothing else had appeared to show that the work had been followed elsewhere.

The writer well remembers the first clinical observations in regard to the Inhibitive test. It was found in the tests of say 100 different patients, that the majority gave little or no "Inhibitive" in single tests, while about 25 gave a moderately marked reaction, now called three plus. Less than one patient in a hundred gave

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a four plus plus or even a four plus. As the months went by, it was observed that those giving such very strong positives invariably progressed exceptionally well, in comparison with those who gave only a moderately marked reaction, and in contrast to those giving only slight or no "inhibitive," who frequently did *not* do well. So that the first value seen in the Inhibitive test was *the prognosis*.

Shortly, a positive Inhibitive occurred in an apparently normal control serum. On request, this normal control submitted to an outside examination (C. D. Parfitt), and tuberculosis was diagnosed. Soon after, a second control gave a positive, and again the individual was found to be tuberculous, this time tubercle bacilli being obtained. Thus, possible value was foreseen in *diagnosis*.

In the next ten years, except during the war, the writer, as clinician and not serologist, working alongside of the originator, watched (introspectively) with keen interest, and indeed with fascination, their mounting confidence in the specificity of the two tests, the Fixation from the beginning, being done with the Inhibitive. Not until after the war did others have a close opportunity to observe these phenomena.

The value of the combined use of the two tests, Caulfeild's Inhibitive and the Tuberculo-complement-fixation, at the same time, was seen in our early clinical observations. It was apparent that each of the two tests was frequently complementary to the other—if one gave no information, the alternate test often did so, that is if there was anything to be informed about. Also, if the one which had been negative became positive, then the other which had been positive not infrequently became negative, or tended to do so. (See Fig. 7, graph of Case 6 "Jef"). This resulted in the separate graph of each, crossing the graph of the other. Thus they were of dual value, and in a sense, one corroborated the other. Similarly if both graphs made a marked move at the same time, from a negative to a positive, the significance of this sign was doubled (See Fig. No. 10, graph of Case No. 16 "M.C." or "Cor," and Fig. No. 12, graph of Case No. 19 "Oli" in the text proper).

It was in 1920 that Caulfeild raised the question, might not these tests be of greatest value in apparently normal contacts, where, without any help from symptoms, physical signs or x-ray picture, the onset of tuberculous disease could be foreseen by immunological reactions? And so the serological facilities of the Connaught Laboratories, University of Toronto, where he was Research Member, were made available for the Toronto Western Hospital O.P.D. Chest Clinic of which I was in charge.

A year or two later, the tests were taken over by Norwich's Lab-

oratories, Christie Hospital, Toronto, of what is now called the Department of Veterans' Affairs. This was at the request of Caulfeild, then and for the next fifteen years, Director of the Chest Clinic of that Hospital. For twenty years therefore this serological work has been under the direction or control of Norwich, and it is to be noted that the latest published technique of the Inhibitive, was by A. C. Norwich et al in 1930.<sup>10</sup> The latter then wrote "the value of these tests will soon become apparent to anyone with the facilities, who has the patience and tenacity." Is it necessary to add that an indefinable attribute called "vision," ("a thing seen in the imagination") must provide the unfailing incentive for the maintenance of the two qualities just mentioned? Caulfeild certainly had vision, and he once declared to his friend that he was constantly driven by incentive. Was it the incentive of vision?

Over a period of thirty years starting in 1908, Caulfeild worked in four different hospitals—the Muskoka Hospital for Tuberculosis, the Toronto General Hospital, Christie Street Hospital and the Toronto Western Hospital. The serological tests were carried out in the three laboratories previously named. By virtue of Caulfeild's posts in these several different hospitals and laboratories, he worked with a different group in each one. This explains the informal team of a score of serologically-minded clinicians and technicians, distributed among several hospitals and laboratories.

The rest of the story and accomplishments to date, are told in the text of the symposium which follows.

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## A Symposium

### A Scheme in Operation Twenty Years

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*in clinical or laboratory collaboration with*

Adrian Anglin, M.D., F.C.C.P.; Col. Milton H. Brown,\* O.B.E., F.C.C.P.; Capt. W. H. Cruickshank;\* Maj. S. J. Forrest,\* F.C.C.P.; Major C. B. Graham;\* Lt. Col. P. W. Hardie,\* F.C.C.P.; Lt. Col. T. G. Heaton,\* E.D., F.C.C.P.; H. I. Kinsey, M.B., F.R.C.P. (Can.), F.A.C.P., F.C.C.P.; Laurella McClelland, M.D.; E. L. Sexsmith, M.B.; Lt. Col. Magnus Spence;\* Margaret S. Thompson, M.D.; T. R. Welwood, M.B., (fifteen of the twenty above are clinicians of T.W.H. Chest Clinic); Dorothy V. Kitchen, Merle F. Bassingthwaighe, Assoc. Serologists.

#### INTRODUCTION

In previous publications,<sup>1,2,3,4,5</sup> we have presented evidence that by means of serological tests it may be possible to diagnose tuberculosis six months to two years before the appearance of clinical signs and symptoms, and, that by the institution of appropriate treatment during this pre-clinical stage, the onset of manifest disease may be prevented. We have found it difficult to convince the profession of the diagnostic value of these tests, but as the average incubation period of tuberculosis is three to five years, it should not be hard to believe that immunological reactions occurring in the body during that time are reflected in the serum. The sequence of events is set out in figure 1.

The tests used are Caulfeild's Inhibitive and the Tuberculo-complement-fixation, together with the Mantoux, i.e. the intracutaneous tuberculin, done every three to six months, depending successively on whether the group under observation are exposed to tuberculous infection or not, and whether their hours of work are long or short.

Tests are recorded in graphs, which, by certain defined reactions and changes, give 6 to 24 months warning of the approach of disease. In such case, additional daily rest of one or two hours is advised and, if possible, enforced. If the hours of work are long, 1 or 2 months complete rest may be considered necessary. By

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\*\*Deceased, 1943.

certain combinations of these reactions we predict or foresee the onset of the disease tuberculosis, and then forestall it by applying additional rest.

The original serological premise of this work was published by Caulfeild as far back as 1911.<sup>6</sup> In 1925 a broader serological and clinical premise was published by Caulfeild's group of seven.<sup>1</sup> Ogden's first efforts to make the clinical application of the tests more practical were in 1930<sup>2</sup> and 1931,<sup>3</sup> while in 1934<sup>4</sup> Caulfeild and Anglin published the most convincing evidence yet, showing by graphs of serial serological tests, how clinical tuberculosis was being forecast. This paper included statistics which indicated a high percentage of accuracy in such forecasting. In 1939<sup>5</sup> a group of ten clinicians showed how they applied the method to "The Abolition of Clinical Tuberculosis by Anticipation and Control." This present paper so simplifies the practical application that any trained clinical and laboratory group can apply it themselves.

Because the purpose of this paper is to demonstrate the simple clinical application of our method, as now being used, and because a dozen publications have previously elaborated upon the premises, the latter have been only tersely named in the paragraph above. Nevertheless, for reasons presently to be given, and so that this symposium may be comprehensive in itself, we have been

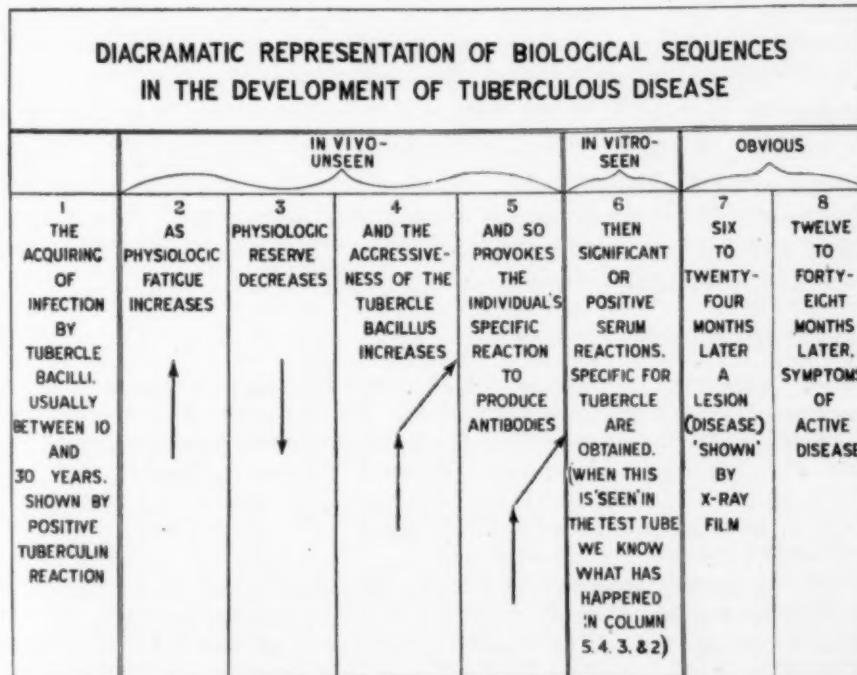


Fig. No. 1, Diagram  
"Diagrammatic Representation of Biological . . ." etc.

persuaded to introduce at this point, some substantial recapitulation from previous publications. A few pages of such, therefore, follow herewith, *the repeated material being in smaller type*. We shall then resume the main theme of this paper, namely, the presentation of our twenty-five year old scheme, brought closer to precision by research in our clinical technique during the past ten years.

With our present defined regular observation and supervision, so rarely does anyone slip through our protective net into tuberculous disease, that we can fairly claim this to be now almost impossible (excepting perhaps into the primary-infection-type). We recall that prior to Caulfeild's death he charged some of our clinical members not to write nor speak as though we believed our tests were 100 per cent efficient, because this cannot be claimed for any biological test.

From scores of critics and friends, through twenty years, has come the charge (though rarely with vehemence), by spoken word or by implication, that, in this or that phase, our work and accomplishments are not understandable. Friends have admonished us to write and tell again, how, where and why, things work out as we say. "Tell about the test itself; why some normals give positives for years; how the tests are reactions of immunity; the closely related logic of their ability to anticipate disease; and the rationale of their variations under stress or ease!"

The answers to most of these questions have already been published in such studied phraseology by a dozen writers, that they cannot be improved upon. Because however they have appeared in various medical journals (and in three different countries, Britain, United States and Canada) which may not be easily available to everyone, we herewith quote, with little regard to sequence, those most frequently enquired about. We also hope to answer here all previously unanswered questions.

#### RE TECHNIQUE OF TESTS

"The T.C.F. as an immunological method is so well known that no explanatory comment seems necessary. The inhibitive test is relatively unknown. It was first reported upon by the originator (A.H.W.C<sup>7</sup>) in 1911. For our present purpose it seems sufficient to state that it is a test-tube reaction with the patient's serum, and similar to complement-fixation in that antigen, serum, complement, and sensitized corpuscles are used."<sup>4</sup>

"The inhibitive reaction is a serological test used to estimate the amount or degree of inhibitin in the blood. Inhibitin is the name applied to certain bodies or qualities found in the blood of tuberculous patients who are resisting their disease well, that is, from a biological standpoint. It must also be accepted that these reactions have reference to some tuberculous antibody only."<sup>8</sup>

"Although the inhibitive test brings together a particular type of tuberculo-antigen, the inactivated serum to be tested, complement, and, after an interval, sensitized corpuscles, the anti-complementary strengths of the antigen used bar it from being regarded as a modification of the T.C.F. reaction."<sup>1</sup>

"The inhibitive reaction was noted by Caulfeild in 1911 while working in serology at the Gravenhurst Sanatoria. In an endeavour to obtain some explanation for the lack of correlation between the results obtained with the tuberculo-complement fixation and the clinical courses, he developed a technique which seemed to be basically different from the detail and type of technique as used for the true tuberculo-complement fixation test. This technique he eventually named 'the inhibitive reaction'. In this test the greater the degree of haemolysis the greater the degree of the inhibitive reaction, a reaction which is the direct opposite to that obtained with the tuberculo-complement fixation test. 'The term 'inhibitive' was adopted because certain non-specific factors were apparently inhibited by the action of the specific tuberculous sera in conjunction with the particular antigen used in this test. Those cases giving a marked degree of haemolysis, that is a strong inhibitive reaction, so frequently showed favourable progress that this correlation was a very striking feature."<sup>2</sup>

"The technique of the inhibitive is more difficult than that of the Wasserman."<sup>3</sup> On this fact a director of laboratories has commented: "our technicians mastered the Wasserman and we can master the inhibitive, even if several times as difficult."

#### RE CLINICAL APPLICATION

"Most who have attempted to use these serological tests elsewhere have found them unsatisfactory chiefly because they did not give the results expected by the physician. In other words, the clinician demands that a satisfactory laboratory test should give about 100 per cent positive results in clinical cases and about 100 per cent negatives in all individuals in whom tuberculosis cannot be demonstrated. Any other result is regarded as indicating the lack of practical value."

"Far advanced cases may give exactly the same type of serological graph as those with minimal degrees of involvement. On immunological grounds there is no reason to expect that positive serological tests should be restricted to that ill-defined group which we label as clinical, and should not be found to an unknown percentage among the tuberculin-positive *normals*. If the same types of positive serological results may be obtained in the far-advanced cases as in those of minimal involvement, it seems logical to infer that similar types of serological results may be obtained in an unknown percentage of apparent normals (who are tuberculin-positive) with a non-demonstrable lesion, which has not been eradicated, irrespective as to its induction of symptoms."<sup>4</sup>

#### ANTICIPATION OF CLINICAL DISEASE

"Their most dramatic value is seen in tuberculosis contacts. By means of positive tests we have diagnosed latent tuberculosis two years before clinical disease and one year before even demonstrable by x-ray. In hydrophobia the incubation period of one month gives us time to vaccinate against the onset of the disease; in the reinfection-type pulmonary tuberculosis with an incubation period of one to five years we have time to forestall the disease."

"Caulfeild said that we place serology alongside of other forms of examination as just another aid. Would we rely on that recent and valuable method of examination, the x-ray stereo-picture, to the exclusion of history-taking or physical examination? The roentgenologists would agree with our answer, 'Certainly not'."<sup>2</sup>

"It is satisfactory to have further definite assistance in diagnosis, even to the point of being able to recognize the disease in the pre-clinical or biological stage, and with this advance (or inside) information, and by treatment or restricted regime, to be able to keep the patient from reaching the stage of evident tuberculosis."<sup>3</sup>

"We know that a positive tuberculin skin test signifies that tuberculous infection has taken place. If, months or years later, symptoms appear, or x-ray films demonstrate a lesion, disease has already developed. Are there any means by which in this *blackout period* we may be informed of such serious transition from infection to disease before it actually happens? We believe that serial serological tests indicate that the infection is no longer dormant and that a transitional stage has been reached which, if unrecognized and untreated will lead to active clinical tuberculosis clearly demonstrable by routine methods."<sup>4</sup>

"Clinical tuberculosis became demonstrable at some time after the initial observation in 43 per cent of individuals who gave a positive or questionable serological graph. It was also found that no case developed tuberculosis without warning of this being afforded by the preceding serological results."<sup>4</sup>

"The appreciation of a pre-tuberculosis stage, detected only by blood serum reactions such as the inhibitive and T.C.F., is not a new conception, having been advocated by one of us (A.H.W.C.) as early as 1911. Heretofore, without these tests we had no means of discriminating between the contacts unless or until they showed positive sputum, positive x-ray, symptoms or signs, and then actual disease was present and it was too late for prevention. To our knowledge, no other test at present in constant use, will specifically anticipate tuberculous disease."<sup>5</sup>

Recently we have been much interested in again hearing J. F. Bredeck, Health Commissioner, formerly Tuberculosis Commissioner of St. Louis,<sup>6</sup> say that for fifteen years he has been doing the same as we, but by other means. He has been correctly predicting the onset of clinical tuberculosis in the individual, by the combined use of the intradermal tuberculin test up to 10 mgm. and the Schilling index.

"Ten physicians of the clinic staff acknowledge frequent aid in anticipating tuberculous disease by positive serological reactions or positive graphs, months and years before evidence of the disease by physical, roentgenological or sputum examination would and did occur, that is, if advice were unheeded."<sup>5</sup>

"Tuberculin positiveness indicates the previous implantation of *B. tuberculosis* and the formation of anatomical tubercle. The establishment of a suggestive number of positive serological results would seem to demonstrate that the individual is on the threshold of, or is actually suffering from clinical disease, and should be periodically examined; the actual demonstration of bacilli or x-ray proof may take years."

"The longest period in a minor from the initial observation, while

the individual was under contact, to the demonstration of disease was 12 years; the longest period in an adult from the first positive tuberculin test was 22 years; the shortest period in an adult (starting as a tuberculin-positive normal) from the first positive serological test was under 2 years."<sup>4</sup>

#### IN WHAT PERCENTAGES ARE THE REACTIONS OF PROVED CLINICAL SIGNIFICANCE?

"Tuberculosis cases as a whole show a much greater incidence of positive inhibitive tests than do the non-tuberculous, 50.4 per cent as against 11.7 per cent; and also, the active tuberculosis cases show more than the quiescent, arrested or cured. The percentage of the non-tuberculous giving positive inhibitive tests would appear rather high, but in view of the fact that necropsy statistics show a large percentage of previously unsuspected patients to have tuberculous lesions, it is quite possible that a number of these (classed as non-tuberculous) have biological tuberculosis."

"Among the active tuberculosis cases the combined reactions, that is, T.C.F. and inhibitive tests, when considered together, have been 100 per cent correct in at least one of three done over a period of four months, and among the quiescent, arrested, or cured cases, 94 per cent correct."

"The proponents of the tuberculo-serological tests have repeatedly emphasized the value of these tests when repeated at intervals of four to six weeks over a period of six months to years, and to anyone with the facilities, who has the patience and tenacity, this will soon become apparent. There are occasions, however, when the single test is of inestimable value."

"The inhibitive reaction of Caulfeild is specific to tuberculous sera. It at any rate appears much more frequently in the proved tuberculous than in the supposedly non-tuberculous."

"The inhibitive reactions of Caulfeild is specific for this disease and, so far, is the best method of estimating its presence."<sup>10</sup>

"X-ray films could not be divided into positives and negatives, either as films or as a measurement of clinical tuberculosis. It is perhaps fatuous to say that the proper measurement of clinical tuberculosis is the function of the clinician. This is admitted insofar as the x-ray is concerned. Our desire is to put the serological graph in a relatively similar position."

It seems not generally known that results in serology on a small group of *normals* have been published.

"Results obtained upon normals, who had been found to be tuberculin-negative, should provide the best type of control to the results obtained upon clinical groups. Thus these results should give an accurate indication of the degree to which the tests gave 'false positives.' In other words, the percentage of laboratory error in individuals who must, with the minimum of reservation, be regarded as yet uninfected with the tubercle bacillus . . . 53 had been found, to be negative to tuberculin. Tabled results show very definitely that clinical cases, on an average, do not give anything like 100 per cent positive results with either of the tests, but nevertheless they do show a marked contrast to what is obtained with tuberculin-negative individuals. In compiling the results upon the clinical cases it was manifest that far-advanced cases may

give exactly the same type of serological graph as those with minimal degree of involvement."<sup>4</sup>

"The T.C.F. was positive in 13 per cent of tuberculin-negative normals. The Inhibitive was positive in 2 per cent tuberculin-negative normals."<sup>4</sup>

#### COMMENT

It should again be made plain that "the means by which we forecast the probable development of clinical tuberculosis in tuberculin-positive individuals (contacts) is through the use of serial serological tests. *Serial* tests have not been used except in Toronto."<sup>4</sup> Even in Toronto, strange as it may seem, serology, much less serial serology, has been little used outside of our own informal clinical laboratory team which has worked largely at two hospitals, the Western and Christie, and at two laboratories, Christie and the Connaught. Nowhere else have they been interpreted and used alongside of knowledge of the sensitivity to tuberculin in the three dilutions used by us, and with information as to the seasonal or holiday variations between the stress and ease of the individuals tested. One would expect immunological tests to react differently under stress or ease when dealing with tuberculous infection.

Referring above to the comparatively little use which has been made of serology even in Toronto district where it has been available, we must add, that some 200 physicians in or about Toronto, in general practice or internal medicine, over a period of 20 years, have come for aid in the three following types of cases: Firstly in contacts, secondly in the diagnosis of clinical disease, and thirdly in the silent "spot," as found in the incidental x-ray, the industrial mass survey and more recently in the army-reject. (We would like to deal with this subject in a subsequent paper).

"Thus, we would seem to be the only group in a position to make a comprehensive fact finding analysis, irrespective of what might be regarded as desirable or of practical value."<sup>4</sup>

We here note that two other Ontario groups, each carried out a careful study along these lines for a period of two and three years, which, in relation to the disease tuberculosis and its latent period, must be considered very restricted. We feel it lamentable that different points of view, or insufficient time and staffs, limited their scope, and then cut short their work.

#### MONETARY VALUE VS. COST OF SEROLOGY

To us doing administrative work, unsupported by those not interested in abstract preventive medicine as contrasted with actual illness, comes the temptation to balance monetary values in cash and time. When the nurse or child under observation happens to

be our own daughter, if the odds are anywhere near 50-50, most parents say, spend the time or the money to prevent.

"Because in ten years no nurse regularly tested has developed tuberculosis without warning from the tests, and no nurse who got warning and heeded it, got tuberculosis, the saving in previous average hospitalization costs for cases discovered by x-ray, has more than equalled the costs of the tests. This is entirely apart from the saving of health to the nurses and the cost of sanatorium care for those who break down."<sup>11</sup>

On the other hand under our scheme, there is likely to be a small undetermined percentage who take the additional rest unnecessarily, that is, who would not have developed the disease even if they had not taken the rest. This is a price we must pay to protect the majority.

#### PLACE IN ANTI-TUBERCULOSIS EFFORT AND ESTIMATED DIVIDENDS

(a) Of greatest value in chest clinics, (b) in differentiating between those liable to develop disease and those who are not; (c) whereas in 100 contacts (say) 15 usually develop the disease, if \$600.00 were invested annually for laboratory expenses (plus transportation charges, work of collecting contacts and specimens, and medical advice indicated,—about another \$600.00 in cost), 10 of the fifteen can be kept well. The latter ten just mentioned as being kept well, and continuing at work, would produce, at \$12.00 per week for 50 weeks—\$6,000.00 in the year. This is 1000 per cent dividend on the annual cash investment (or 500 per cent dividend on the total cost). The whole of this saving would, of course, not be evident until after three, four or five years—the usual period of time after infection required for disease to develop, without the protection of the tests and the advice indicated. The above does not include any estimate of dividend from saving of sanatorium costs.

Most health workers find so much to do in the way of helping sick people get well, that it is difficult to give time or thought to preventing that illness, even though it may be obvious that the saving of sanatorium cost for two or three would pay the monetary outlay in the observation of a hundred potential cases. It is as though we were so busy repairing those who have fallen over a precipice, that we have no time to go to the top to prevent others from falling.

#### IN DIAGNOSIS

We have referred in a paragraph above to possible aid in the diagnosis of clinical tuberculosis; this must be qualified.

"Because more than one or two serological tests at intervals of a month are frequently needed to derive full value from them, this delay constitutes *a deterrent in their use as an aid in the diagnosis of actual disease*; neither patient nor physician is content to wait for diagnosis when the patient is already ill. The place of these tests *in diagnosis* of clinical disease is to supplement the recognized procedures, including history, symptoms, physical examination, tuberculin skin test, sputum examination and x-ray film, and all of these six methods should have been tried first."<sup>12</sup>

"These serological tests rarely make the diagnosis. Their function, if employed in an effort to diagnose clinical disease, is to indicate the need of tests of greater diagnostic value, particularly the x-ray (T.G.H.). Nevertheless, all other methods failing, particularly in early diagnosis, (not uncommonly in adenitis, peritonitis, epididymitis, phlyctenular conjunctivitis, pleuritis, erythema nodosum, and inflammatory conditions of bone, joint and pelvis), aid from serology is at times dramatic."<sup>13</sup> "The inhibitive reaction is a valuable aid occasionally in diagnosis."<sup>10</sup>

#### SILENT OR OCCULT LESIONS

Also "the finding by x-ray of a symptomless or 'silent' lesion, pre-clinical or subclinical, at once requires a decision between activity and inactivity, particularly without an identical picture 5 or more years previously, or without a clear film within the previous one to five years."<sup>13</sup>

"A pressing need in our diagnostic procedure is some means of judging more accurately the degree of danger to the patient in existing but small or occult lesions."<sup>14</sup>

"Relatively little is known at present of subclinical disease or of methods for its discovery. The problem of the early pulmonary infiltrate is to determine whether it is pathologically active or healed... reliance usually has been placed on serial roentgen-ray films, but... a process may be active... and yet may show no significant roentgen-ray change for a period of years."<sup>15</sup> "Here again our group of a dozen feel that we have in serology the earliest accurate answer. The profession at large may more readily accept this as being possible with a manifestly abnormal shadow already visible. When, however, they read our statements that we can anticipate the disease and its shadow by six to eighteen months, that is just too much; it seems incredible until they see it demonstrated."<sup>13</sup>

#### RE SURVEYS

"In many surveys throughout the country in the past fifteen years tuberculin-testing has been used as a fine 'screen to distinguish between those individuals who have been infected with tubercle bacilli and those who have not'<sup>16</sup> (school and hospital nurse surveys). "The x-ray film is then used as a further screen, finer than physical examination, to pick out even the minimal lesions that may be among the tuberculin-positives." "Most of these x-ray films of persons with positive tuberculin tests will show no tuberculous lesion. It is desirable therefore to have some means of foretelling which of these tuberculin-positive individuals are liable to develop the disease and which are not (T.G.H.). In this regard there are two serological tests that are the finest screen available to make this differentiation."<sup>13</sup>

When 2,000 High School children are tuberculin tested, and 200

give reactions, they are x-rayed and (say) two are found with lesions. Instead of waiting a year or two to repeat the x-ray film of the remaining 198 reactors, if they were blood-tested 2 or 4 times yearly, the approach of a tuberculous lesion could be foreseen and forestalled in the majority of cases. This is what we have been doing with our contacts and tuberculin positive nurses (as all tuberculin positive individuals must have been contacts).

"In our hospital School for Nurses we do not wait for an annual x-ray film to demonstrate a lesion in its early stage, when, of course, it is too late for prevention. We are anticipating disease by biological tests and precluding it by extra hygienic care."<sup>5</sup>

#### EVOLUTION OF PRESENT USE OF THE TESTS

"In the periodic observation of tuberculosis contacts, a small group of physicians working on this problem at the Toronto Western and Christie Street Hospitals, have familiarized themselves with the use and interpretation of these dual serological tests. Not only has this group had access to these tests since 1920, but also, several consecutive years' use of them in the same several hundred patients, without which no one can see for himself their specificity and full value. None of this group except the originator gave them credence in the first year of their use. How could the prediction of a disease by a biological test be proved or disproved in less than two years' trial, when the average incubation period of that disease is from three to five years, i.e. the average interval of time between intimate exposure to gross infection and the usual clinical diagnosis?"<sup>13</sup>

One of our group (T.R.W.) tells that he worked daily for eighteen months in the chest clinic at Christie Street Hospital where these tests were in constant use. He states that he became convinced of their specificity and value while at that clinic.

The nearest to drama in the evolution of the whole work has been the appearance of definite tuberculous disease in individuals where, for the previous one, two or four years, there had been nothing but serum reactions to suggest that this was taking place. The first series of such individual episodes was at a veterans' hospital where pensioners were repeatedly examined and tested year after year. The second series was at a large O.P.D. chest clinic of a general hospital (T.W.H.) where, starting in 1920, known tuberculin-positive contacts, giving significant serological reaction, were followed into the second, third and fourth years. When the disease appeared in case after case, in which serological tests had given warning in advance, it amounted to a revelation to those who had not previously observed this phenomenon.

#### THE RATIONALE

The blood serum of patients with active tuberculous disease gives a high percentage of significant reactions to Caulfeild's In-

hibitive and/or the Tuberculo-Complement-Fixation tests. So also the serum of grossly infected tuberculosis contacts who are liable to develop disease, gives the same positive reactions, for a year or two prior to the development of a lesion demonstrable by x-ray, and for a longer period before symptoms. Thus, these laboratory tests provide us with the unusual means of anticipating actual clinical disease.

The logic of this would not be evident with any other disease, nor with any other tests. No other disease except leprosy has as prolonged an incubation or latent period, and no other tests are really immunological. Depending upon the balance between the amount of *tuberculous infection* received and the *physiological reserve* of the individual, the incubation period will be short or long. (Our re-infection type cases with the shortest incubation periods have usually been known to have received the heaviest dosage of infection). If and when the attacking infection gains the ascendancy, the individual's specific immunity to tuberculosis is stimulated, and is made manifest in the above mentioned immunological reactions, the Inhibitive and the Fixation. By being thus informed of the approach of disease from 6 to 24 months ahead, we have ample time by additional rest, to *reverse the relative strengths of the physiological reserve and the attacking infection*, and so prevent actual disease.

Because we have blood serum tests which are specific for tuberculosis, and are immunologic, and because the average incubation period of this disease is now known to be three to five years, it is logical to expect that, while the disease is still in the preclinical or biologic stage, the defences will be reacting against its onset. It is not illogical therefore, that these tests are found positive for six months to two years prior to the development of clinical disease. Neither is it surprising to hear, that, with this advance information, further development into clinical or manifest disease can be prevented, if that form of *treatment long known to be specific for tuberculosis, namely rest, be applied, even in fractional daily doses*.

During the long incubation period peculiar to Tuberculosis, the immunological process present may be detected and its course discerned by Caulfeild's Inhibitive and Tuberculo-Complement-Fixation reactions from six to twenty-four months prior to the development of a lesion demonstrable by x-ray, and for a longer period before symptoms appear. Hence we have the unusual facility, by means of these serological tests, of anticipating clinical disease, thus gaining the time factor so important in arresting or preventing development. Owing to the prolonged incubation period of tuberculous infections in contrast to that of other dis-

eases, this immunological phenomenon is present only in tuberculosis. (A.C.N., M.F.M.).

The comparability of our immunological tests to armed forces, was recently described by two of us (O. & A.) in semi-popular vein, the allegory being told in dialogue form.

"Patient: 'You tell me my tests show that I am fighting the infection and that this, in turn, means that the infection is active, so that I am in danger of developing the disease. Could you explain?'

Doctor: 'If you knew that there were armed forces in another country, and you further learned that those forces were moving with rapidity, you might reasonably anticipate war, the world knows that today, (coincidentally published on Sept. 1st, 1939, the day of the outbreak of war). We do two tests of your blood serum monthly or quarterly, looking for reactions that take place with the serum of patients actually fighting tuberculous disease. These reactions are evidence of an effort by the defense mechanism of the body to make the patient immune (M.H.B.) and so are what might be called immunologic, resistant or fighting-back reactions. They are comparable to armed forces. That is the allegory. Those lines on your chart make what we call a graph and they show the degree to which your tests may be positive, whether they are moving or not and, if moving, how rapidly. One test seldom tells the whole story, e.g. it cannot tell whether or not the reactions are *moving*. Both your reactions have been over the positive line—or normal boundary—and both are moving rapidly. A fight is on; the warning could not be more plainly written.'<sup>17</sup>

If nothing is known about an army designated "A," but if it is known that an opposing army "B," is in marked movement (Whether forward or backward does not affect the immediate problem), then it can be surmised that army "A" is, or has recently been active. Just so, in the presence of unrecognized latent tuberculosis, if immunological reactions are on the move (in either direction), then activity or recent activity of tubercle bacilli can logically be assumed.

#### REVIEW OF HIGHLIGHTS

The basis of the work is in three main points:

- (a) that the average incubation period of the disease tuberculosis is now known to be from three to five years;
- (b) that we have serum tests capable of anticipating manifest disease by one or two years, that is, in the pre-clinical stage;
- (c) that in this pre-clinical stage, when discerned by the tests, the development of actual disease is prevented by the addition of fractional daily amounts of rest (a thousand times easier to prevent than to cure).

The ready understanding of this new procedure is *impeded by the following factors:*

- (a) The long incubation period of tuberculosis is not yet generally known, and so observers are impatient;
- (b) The anticipation of disease is new;
- (c) A small percentage of apparent normals give positive tests for years; it is forgotten that a similar small percentage of the apparently non-tuberculous, are found tuberculous at necropsy;
- (d) The rationale of the variability of reactions in positive cases (and also in tuberculin positive contacts) is not very obvious. Being immunological, the reactions vary with the changing stress and relaxation of life. As our physiological reserve and fatigue vary, so in turn the aggression or invasiveness of tubercle bacilli is accelerated or impeded, which again in turn produces variations in the specific immunological tests, then seen in the laboratory reactions (see diagram of biological sequences at the beginning of this paper).

There may be some who do not comprehend the rationale or principle of the longer known of these two tests, viz., the Fixation reaction. Even so, we seldom now hear the charge that it cannot be explained. However, to mention the newer test, the Inhibitive, in certain quarters, is to provoke head-shaking or silence, intimating very definitely the accusation that it is not understandable. The principle underlying Caulfield's Inhibitive Reaction is not more obscure than that of other serological tests. Moreover, up to the present time, lack of a detailed knowledge of the serological processes involved has apparently not deterred members of the medical profession from availing themselves of any assistance obtainable from such sources. It may be assumed that the average medical practitioner is more concerned with the diagnostic value of a test than with the processes involved in obtaining the results.

"Over a period of 15 years a total of 1,300 known contacts, tuberculin-positive, and 400 normals, have been under observation. Of those who followed our prescribed scheme not one has developed tuberculosis. When the contact series includes those whose observation was irregular, only 4.15 per cent (54 out of 1,301) of the total did develop the disease. The incidence in other contact series ranges from 10 to 40 per cent, averaging 20 to 25 per cent.<sup>18,19</sup> Even when the normal series includes those the observation of whom was irregular not one of the 400 acquired the disease. The incidence among normals in the Framingham survey was 1 to 2 per cent."<sup>5</sup>

In our School for Nurses it was found that one could fairly predict a case or more of tuberculosis within a year or two following a let down in the required testing, such as might be occasioned by lack of strict adherence to the prescribed routine, or even the

absence of the staff nurse in charge of testing, for a month. (This latter contingency would enhance the possible development of only the primary-infection-type, such as Case 28 (S.R.), where the incubation period can be short).

Since the above findings and figures were published, over 500 additional nurses and half that number of tuberculosis contacts (lack of funds has curtailed the use of serological tests in our O.P.D. Clinic), have come under our serological observation. Our findings and results have continued as before,—in 20 years regular testing of over 2,500 tuberculosis contacts and nurses, no case has developed without previous serological warnings (one exception to date—nurse E.B. developed a minimal apical lesion without any warning in her serological graph), and none where the prescribed extra rest periods have been taken.

The number of dual tests done to December 1939 was 48,592, to date the estimate is 60,000; the number of different patients tested to December 1939 was 21,615 and to date the number is over 25,000 (M.F.M.).

#### PLAN OF TEXT OF THE PRESENT PAPER

We now present:

- (1) Interpretation of the tests,—Caulfeild's Inhibitive and the Tuberculo-Complement-Fixation, in the style of simple arithmetical addition; rules by which certain reactions, graphs or combinations of the same, must be read as Danger Signs.
- (2) Table of rest periods prescribed for the different degrees of serological warning.
- (3) Examples of the ideal or safe type of graph, referred to in rules 9 and 10, including "E.R." with two minimal healed lesions on admission, no extra rest required.
- (4) Examples of Danger Warning graphs, in which the appropriate additional rest was prescribed and taken successfully, that is, each graph became straight or negative or both, and no tuberculosis developed.
- (5) Examples of Danger Warning graphs where appropriate rest was not taken, and where tuberculosis did develop.
- (6) Tuberculin testing, means for greater accuracy in dosage, frequency, timing and interpretation.

#### RULES FOR THE INTERPRETATION OF TESTS

The tests are done every four months, and oftener if danger is in sight. Ten points in the interpretation of a serological graph are given herewith; the first seven are *DANGER SIGNS*, in the order of increasing significance. Numbers 9 and 10 describe graphs

which show no danger. Please refer to graph of Case 1 on a subsequent page at the beginning of the examples.

- (1) Increased sensitivity to tuberculin.
- (2) Two moves of two spaces by either C.I.\* or T.C.F.\*\*; the moves may be either upward or downward.
- (3) Repeated positive T.C.F. with moves (either up or down) of two\*\*\* spaces between the positives.
- (4) Repeated positive C.I.
- (5) Two moves of two spaces by both tests is most significant.
- (6) The more marked the move (changes) in the graph, the greater the significance, or danger.
- (7) With repeated positives in both tests, and with graphs moving rapidly, disease is likely to be impending or present.
- (8) Reactions which are 2 plus and stronger are arbitrarily called positive, although as noted above, certain combinations are of greater significance than a positive reaction *per se*.
- (9) "The ideal or safest type of graph is well below the positive line, does not vary more than one space up or down, and is therefore straight and level or almost so." (As examples see Fig. 2, Case No. 1 "Far" and Fig. 3, Case No. 2 "Web").
- (10) "Just as safe, is any positive *fixation graph* (shown in x's) that does not vary, but continues in a straight line. It must be noted however that the *Inhibitives* (shown in o's) must remain at or next to the negative base line."<sup>20</sup> (Example seen in Fig. 4, Case No. 3, "Dix").

The significance of changes in serological reactions in successive tests, is comparable to that of successive electrocardiograms. "Following occlusion, the area of injured muscle undergoes change from day to day. This is reflected in the electrocardiogram, but each patient will be found to differ in regard to the speed with which this variation takes place. . . . For this reason, several studies are advisable."<sup>21</sup>

In illustration of our system we will present examples of the application of serology. We first show graphs which gave no Danger

\*Caulfeild Inhibitive.

\*\*Tuberculo Complement Fixation.

\*\*\*To put this into laboratory terminology as regards the T.C.F., a reaction of "one plus" means the fixation of one unit of complement; "three plus" means the fixation of two units; and "four plus plus" means the fixation of three units of complement. Therefore a move of one space up or down in the graph means that in the interval of one or two months between the tests some change has taken place in the patient's serum, in that it now fixes half a unit more or half a unit less than previously. Observation over a period of twenty years has taught us that this slight change *per se* conveys no appreciable significance. When, however, there is a change of a full unit in the amount of complement fixed, this does imply significance. This is the basis of our "two space" yardstick referred to.

Signals (safe graphs), no extra rest needed. We then show or describe graphs which gave Danger Warning Signs either in the first several tests, or during a certain period of months of a prolonged observation. In each case the individual took the additional rest advised, the Danger Signs on the graph promptly disappeared, and no tuberculosis developed. It cannot be proved from individual cases, that tuberculosis would have developed, had the individual not followed our advice; we feel however that the proof that this is so, is found in our figures for the series.

Further proof that our theory is correct, that serology gives the warning which must be heeded, can be provided in the *histories of many cases who failed to take the warning and who subsequently developed the disease*. In showing some of the latter cases, it is to be noted that they were followed only because of serological warnings, and that all of them were diagnosed in a minimal stage.

We herewith give the table of serological warnings with their corresponding prescriptions at present in use at the T.W.H. Training School for Nurses:

**TABLE OF REST PERIODS PRESCRIBED FOR THE  
DIFFERENT TYPES OF SEROLOGICAL GRAPHS**

| <i>Serological Warnings</i>  | <i>Corresponding Prescriptions or Advice</i>   |
|--|--|
| Graph "A" signifies:<br>No warning. Prescribe:                             | No restrictions.   |
| Graph "B1" signifies:<br>Caution. Prescribe:<br>with 1 D.S.*               | Daily two and one half hours off, to be resting and sleeping hours; minimum of late leaves; restrict extramural activities and spare her energies in off hours, for three months.  |
| Graph "B2" signifies:<br>Very slight warning.<br>Prescribe:<br>with 2 D.S. | Administration (School for Nurses) to make sure of nurse sleeping in her time off, and no late leaves for three months.  |
| Graph "C" signifies:<br>Slight warning.<br>Prescribe:<br>with 3 D.S.       | Four hours off daily, instead of two, for three months, as above, to be used for sleep.  |
| Graph "D" signifies:<br>Definite warning.<br>Prescribe:<br>with 4 D.S.     | One month at home, mostly as bed patient. In the first week sleep it out, take <i>the whole week in bed</i> to become completely rested. In the second, third and fourth week, three quarter day bed patient, being <i>four hours only, up</i> : 9 to 1, 10 to 2 (sleeping 1 to 3 or 2 to 4) up 3 to 7 or 4 to 8 or occasionally 6 to 10. May play one set of tennis, nine holes of golf, or may do one hour's riding, swimming, skiing, skating, sleighing or tobogganing or moderate work, or two hour's walking (preferably in the open air and in sunshine), i.e. moderate non-competitive exercise. No late evenings, never out of bed after 10 p.m.; this is |

*Serological Warnings*

Graph "E" signifies  
Marked warning.  
Prescribe:  
with say 5 D.S.

Graph "F" signifies:  
Very marked warning;  
disease likely impending.  
Prescribe:  
with say 6 D.S.

\* D.S.=Danger Signal.

*Corresponding Prescriptions or Advice*

not a holiday; it must be a thorough rest or it will not accomplish the needed physical and physiological benefit.

Two months mostly as bed patient as above; first two weeks bed with bathroom privileges only. From 3rd to 8th week inclusive, three-quarter of the day in bed, up only four hours as in "D".

Three months as above, first four weeks as bed patient, bathroom privileges only, then 4 hours up daily.

The above prescriptions "D" to "F" include, where possible, full and balanced diet containing the more valuable constituents, meat, milk or cheese, greens, the visceral meats and the four chief vitamins (preferably in foods). Prescriptions "D," "E" and "F" also assume immediate questioning and examination by x-ray films to make certain that disease is not already present. If the film taken here is suspicious, stereos are taken, and repeated at the end of the one, two or three months.

These prescriptions are reckoned as for nurses having been on full day, eight hour duty, and possibly exposed to reinfection. If a nurse has recently been off duty for a month or more, resting, and in bed for other medical or surgical reasons, this rest period may logically be applied to cancel the need for an additional period of rest. Copy of the prescription ordered is to be forwarded to the parents with short explanation, when the nurse is sent home for the rest period.

**EXAMPLES OF THE IDEAL OR SAFE TYPE OF GRAPH,  
REFERRED TO IN RULES 9 AND 10, REQUIRING  
NO ADDITIONAL REST PERIODS**

Case 1 (Far): Entered nursing school Sept. 1939, negative to 10 mg. tuberculin, with negative Inhibitive and negative Fixation. In Jan. 1941, 10 mg. gave 15 x 20 mm. areola, and in May 1941, 1/20 mg. gave 60 x 45 mm. areola and 20 x 18 mm. induration. Next month, June 1941, one of the serum tests, the Fixation, showed a one space move only, not reckoned as a danger signal. It remained so for four successive tests, then reverted to negative in March 1942, and both tests remained so. This nurse went through the three years with a change in tuberculin sensitivity from being nil to 10 mg., to being markedly sensitive to 1/20 mg. but with no real danger signals in her serologic graph; it was the ideal or safest type of graph; there were no extra rest periods and no tuberculosis. (See Fig. 2 Graph, Case 1).

In the graphs above, horizontal lines have the same terminology as for Wassermann reactions: negative, questionable, 1+ and 2+; positive 3+, 4+ and 4++. Inhibitives are shown thus: o—o; fixations: x—x.

A serological graph labeled "Web" of Case 2 (not described in detail), is reproduced herewith, as being more commonly found, though not as perfect as that in Case 1 (Far) described above. (See Fig. 3 Graph, Case 2).

Case 3 (Dix): Commenced training Feb. 1938 with an 18 x 15 mm. areola to 1 mg. tuberculin, negative C.I. and 4 plus plus (i.e. very strong positive) T.C.F. Tuberculin sensitivity increased to 30 x 20 mm. areola and 8 x 8 mm. induration to 1/20 mg. in Jan. 1941. In Oct. 1940 the C.I. had shown a one space move upward, returned to negative in Feb. 1941 and stayed at negative, while the T.C.F. remained a 4 plus plus, but stationary. We have had no reason to consider this type of graph other than safe (defined in rule No. 10). She graduated without taking any extra rest periods and without tuberculosis. (See Fig. 4 Graph, Case 3).

### IDEAL GRAPH IN HEALED LESION CASE, REQUIRING NO EXTRA REST

Case 4 (E.R.): Bilateral minimal apical lesions were found on entering the school Oct. 1940; on one side the shadow was rather soft, on the other somewhat hard. The outer zone of the left first anterior intercostal space was largely filled with a density constituting 40 per cent opacity and of  $1 \times 1\frac{1}{3}$  inch diameters; the outer zone, right first anterior intercostal space contained a density of  $\frac{1}{2} \times \frac{1}{2}$  inch diameters, consti-

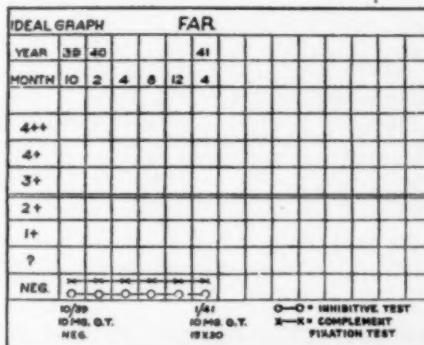


Fig. No. 2, Graph  
Case No. 1 (Far)

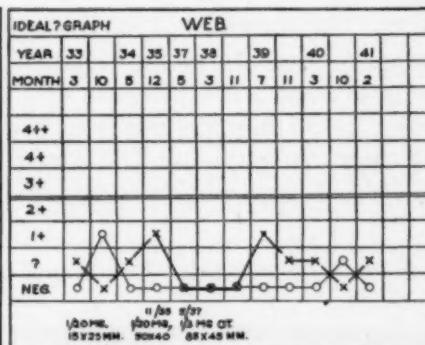


Fig. No. 3, Graph  
Case No. 2 (Web)

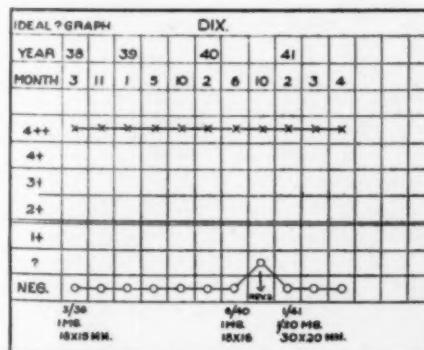


Fig. No. 4, Graph  
Case No. 3 (Dix)

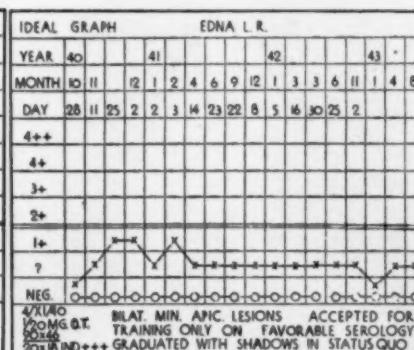


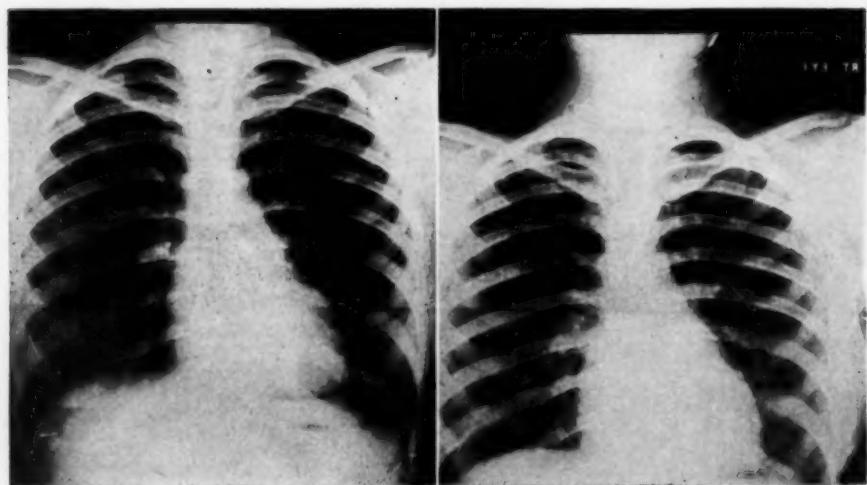
Fig. No. 5, Graph  
Case No. 4 (E. R.)

tuting 30 per cent opacity. Tuberculin 1/20 mg. gave 90 x 76 mm. areola with 20 x 18 mm. induration three plus. At this point the ruling was that the girl would be refused training. The serological test however was dual negative, and because of this, we decided that the lesions were not potentially active, and might be even "cured" or "obsolete". We know of no other hospital which would have dared do what we then did. We advised that she be allowed to remain, with a promise from her that she would retire gracefully if her blood tests showed danger ahead, when she got well into the strain of the long hours and hard work. The tests remained negative, successive films showed no change in the lesions and the nurse has now graduated. Chest films and graph shown herewith. (See Fig. 5 Graph, Case No. 4. Also Illustrations No. 1, chest film, Oct. 1940 and No. 2, chest film, Oct. 1943).

#### TEN GRAPHS WITH DANGER SIGNALS REMEDIED BY REST

These ten Danger Warning graphs became safe after the prescribed additional rest was taken. *The Danger Signs can be seen at first glance.* Seven were known contacts to positive sputum cases, while the remaining three were nurses on hospital duty. In the seven contacts the Danger Signs showed themselves at the beginning of the graphs, and soon disappeared when the rest was taken. The longest graph, that of a nurse, showed no Danger Signs through several years. When Warning Signs appeared, prescriptions of rest were ordered and quickly added to, the last period being a full month bed rest. The Danger Signs abated, the nurse returned to duty and the graph has remained safe. None of the ten individuals have developed tuberculosis.

**Case 5 (Arn):** On admission to the School, Sept. 1939, 1/20 mg. tuberculin gave 92 x 50 mm. pink areola and 20 x 15 mm. induration; C.I. was



Illus. No. 1, Oct. 1940  
Case No. 4 (E.R.)

Illus. No. 2, Oct. 1943  
Case No. 4 (E.R.)

2 plus and T.C.F. 3 plus. In Jan. 1940 C. I. moved down 2 spaces and up again in June 1940. This made 2 D.S.P.'s (Danger Signal Points). In Aug. 1940, the T.C.F. dropped 2 spaces; repeated next month, Sept. 1940, the T.C.F. moved up 4 spaces, and C.I. up to 3 plus. These changes added two D.S.P.'s by the T.C.F. and one by the C.I., totalling five D.S.P.'s. Prescription "F" (3 months rest) was at once ordered for this nurse, and the details of the prescription were strictly followed. On return to duty in Jan. 1941, the T.C.F. had returned to 3 plus and the C.I. down to negative, and both remained so. No tuberculosis developed. Example of precarious graph remedied by advised rest. (See Fig. 6 Graph, Case 5).

**Case 6 (Jef):** Another nurse entered the school with the danger signal of a positive Inhibitive test. From the standpoint of avoiding tuberculosis, it was fortunate that she had to return home for 13 months because of trouble with her feet. In this case the orthopedist assumed the onus of ordering her to quit.\* Returning to the school, the more dangerous (red lined on the lantern slide) Inhibitive graph had gone down, and remained down, while the Fixation had gone up and remained up and stationary throughout her entire course. No more danger signals, no more rest periods and no tuberculosis. Example of a precarious graph remedied by enforced rest. (See Fig. 7 Graph, Case 6).

#### EXAMPLES OF CASES WITH DANGER WARNING GRAPHS, NOT APPROPRIATELY TREATED OR WITH IRREGULAR TESTING, AND WHERE DISEASE DID DEVELOP

A typical case history in four sentences where the indicated rest was not taken and disease developed:

By a positive Mantoux test, a known tuberculosis contact is proved to have been infected. Serial serological tests are then employed and in a month or so our rules for interpretation tell

\*When the clinicians, who are directing the prevention of tuberculous disease among our nurses-in-training, find themselves concerned about a serological warning in regard to any one nurse, they are not without some sense of relief upon hearing that that same nurse has just been ordered off duty for some such operation as appendectomy. The surgeon has assumed the onus of reducing the working staff by one nurse, and for a reason much more easily understood than our new hypothesis.

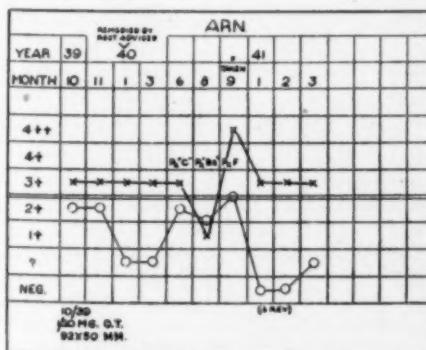


Fig. No. 6, Graph  
Case No. 5 (Arn)

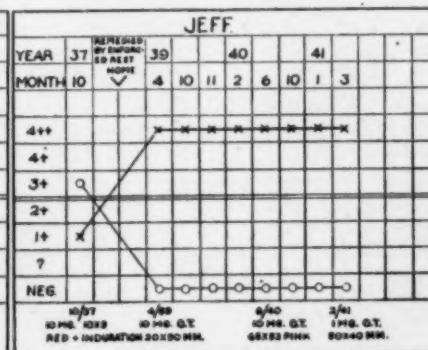


Fig. No. 7, Graph  
Case No. 6 (Jef)

us that the contact is in danger of developing the disease unless extra rest is taken. Chest x-ray films are thus far clear. For one reason or another, the advised rest is not taken, and in one, three or five years (occasionally not for ten years), a periodic x-ray film demonstrates a lesion, or if not under observation, the individual develops frank active tuberculosis.

Three or four score of such cases could be given in detail, observed for two reasons only, that they were contacts, and that their blood tests were positive. One, two or more chest films were clear, and then, where the prescribed rest was not taken, disease was usually demonstrated in a subsequent film. Case No. 15 (Lat) is a simple illustration of plain warning, shown on the graph (reproduced below) in 3 Danger Signs, (D.S.) as defined in rule number 3 given above. The case was a wife whose husband had advanced disease with positive sputum Jan. 1925, and he had coughed since Sept. 1924. In her first serological test, Jan. 1925, the finding of a (3 plus) positive fixation was of little significance *per se*, because as stated in rule 10, a positive fixation graph that remains stationary in subsequent tests and forms a straight graph, is considered safe, and until a second test is done, there can be no graph to provide such information. When however, it was followed by a move of two spaces in the graph in May 1925, then the positive

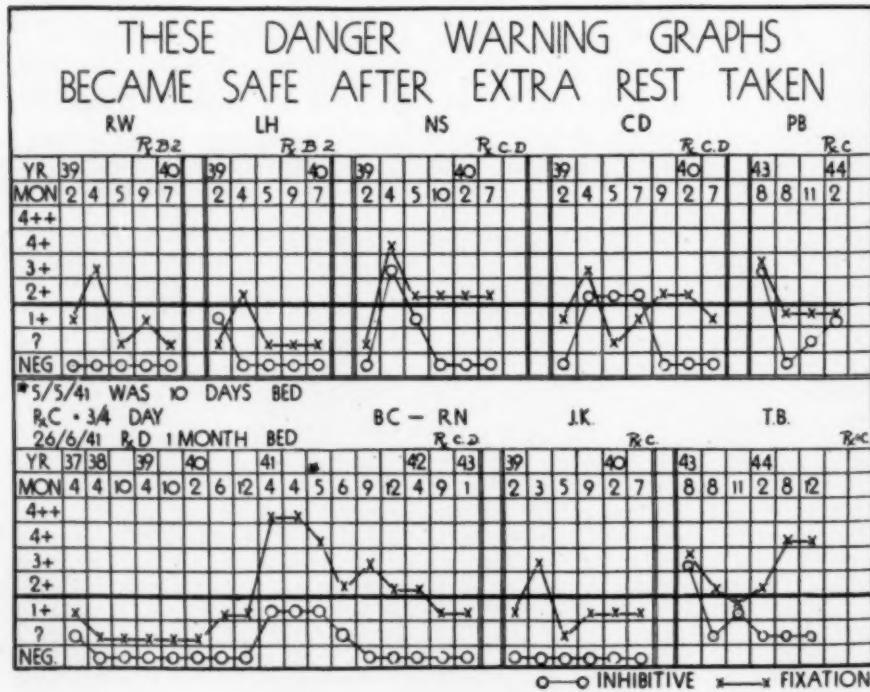


Fig. No. 8, Eight Graphs, Cases 7 to 14  
"Danger Warning"—became safe.

fixation at once assumed significance as the first warning. The move itself, just mentioned, in May 1925, made a second warning, and in October 1925 a further move made a third warning.

The occurrence of the second serological warning in May 1925, plus the knowledge that the wife had not seen fit to take extra rest, prompted an x-ray of her chest in the same month, shown herewith. It was clear. The occurrence of the third warning in October 1925, was followed by a second x-ray film, shown herewith, also clear. In May 1926, a third x-ray film was taken, showing a definite parenchymal lesion occupying the area between the left 1st and 3rd anterior ribs; chest roentgenograms shown herewith. (See Fig. 9, Graph of Case No. 15 "Lat", also Illustrations Nos. 3 and 4, chest films, Case 15).

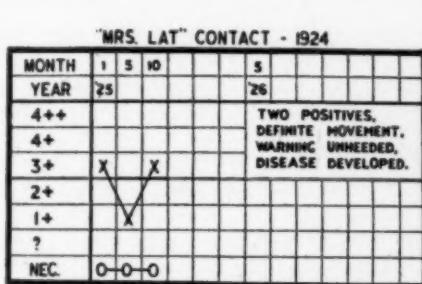


Fig. No. 9, Graph  
Case No. 15 (Lat)

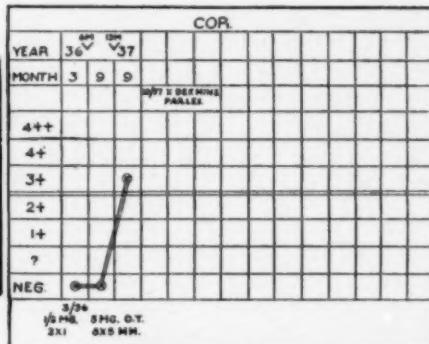
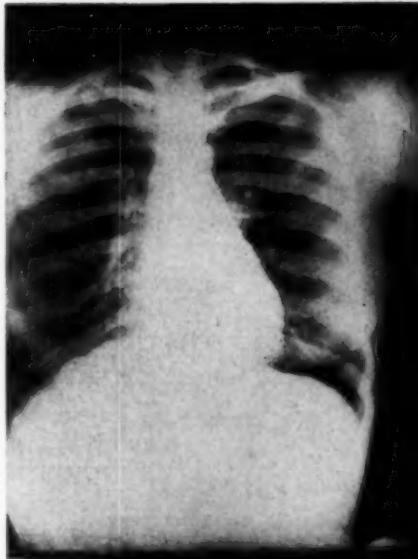


Fig. No. 10, Graph  
Case No. 16 (McC)



Illus. No. 3, May 1925  
Case No. 15 (Lat)



Illus. No. 4, Nov. 1925  
Case No. 15 (Lat)

Case 16 (M.C.): Example of *insufficient testing*, where an interval of 12 months had inadvertently elapsed without tests. Whereas both C.I. and the T.C.F. had previously been negative, both were now positive. The staff nurse in charge at once wrote the order which she had learned was indicated in such cases, namely a month's bed rest, and we signed it. A film was also ordered as usual to make certain that there was not already a lesion. We were too late. The order for a month at home was changed to one for a year in Sanatorium.

Serological Graph labeled "Cor" is that of Case 16 (M.C.). (See Fig. 10 Graph, Case 16).

Case 17 (McC.): This nurse came to our hospital office Nov. 6, 1939 and reported that she had gained 12 lbs. on her recent holiday and had never felt better in her life. In the next week, routine x-ray film revealed that the 1st and 2nd left interspaces were filled with patchy mottling; chest roentgenograms are shown below. An order was at once written: "Miss McC. off duty and to bed; may we see her parents?" Several days later in Principal's office, with parents and nurse also present, the conversation was as follows:

Doctor: Question: "Were there any warnings, if so, since when?"

Nurse: Answer: "Yes Sir, several, since May 1938."

Q: "Was anything done about them?"

A: "Yes, but not exactly what was at first prescribed; 3 weeks restful holidays were taken both last year and this, instead of a month's rest twice, as well as holidays."

Q: "I see the written instructions for the last holidays state 'first week total bed rest.' Was that taken?"

A: "No, but I was in bed until noon every day."

Q: "And out half the night?"

A: "Yes Sir."

Q: "Until twelve?"

A: "Yes Sir."

Q: "Until one?"

A: "Yes Sir."

Q: "Two?"

A: "Not every night."

Q: "Six nights out of seven?"

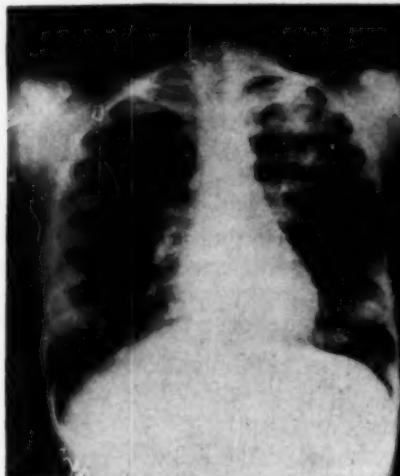
A: "Yes Sir."

Example of evasion on the part of the nurse, and of leniency on the part of the doctors. (See Illustrations 6, chest film and 7, chest film, Case 17).

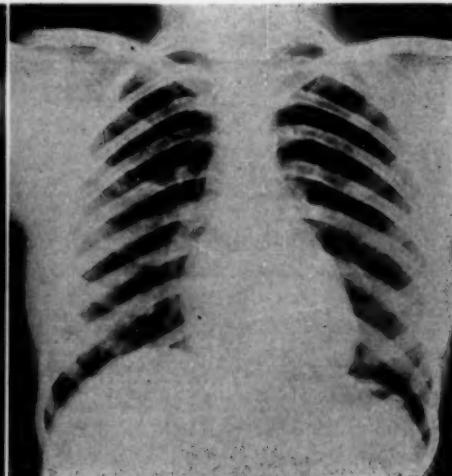
Case 18 (Man): On entering training school Sept. 1938, this nurse was negative to 1 mg. tuberculin, gave 10 x 15 mm. reaction to 5 mg., and negative Inhibitive and Fixation. By Feb. 1939, there was a serological warning by both tests, 3 plus and 4 plus respectively, and in July the tuberculin reaction was 20 x 30 mm. to 10 mg. Four weeks bed rest, *plus* the usual 3 weeks holiday was prescribed that summer, but instead, we compromised with four weeks rest. In Feb. 1940 there was noted markedly increased sensitivity to tuberculin, viz. 120 x 83 mm. to 1/20 mg. By June 1940 there had been two more warning moves by the Inhibitive and also two by the Fixation. Two or three months' rest (designated as prescription E. or F.) was advised, but because of difficulty in taking a rest period at home in this case, a second compromise was allowed

at one month (D). She returned to duty in July, and was posted for her usual annual 3 weeks holiday in August. This was begged off, and again we acquiesced—the third compromise.

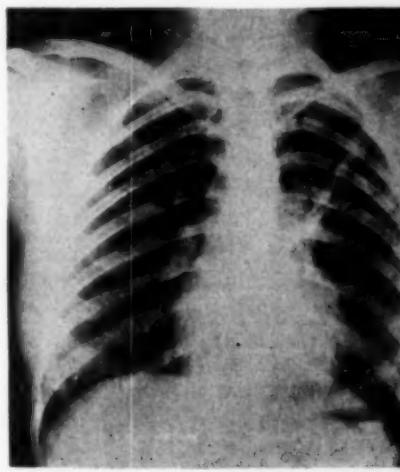
The two guiding clinicians now felt that their efforts to get sufficient periods of rest had been definitely thwarted through 20 months of serological warning, and that the time was now passing or passed, when actual tuberculous disease could be forestalled or prevented by any short period of rest. X-ray films were being taken quarterly as it was feared a lesion would probably appear any time. The nurse was advised, however, to inform us if opportunity for a rest period presented itself. In December 1940 we were informed that a month could be taken without difficulty, to which we replied that nothing less than 3 months, "F", gave any promise of prevention. This seemed so impossible from her



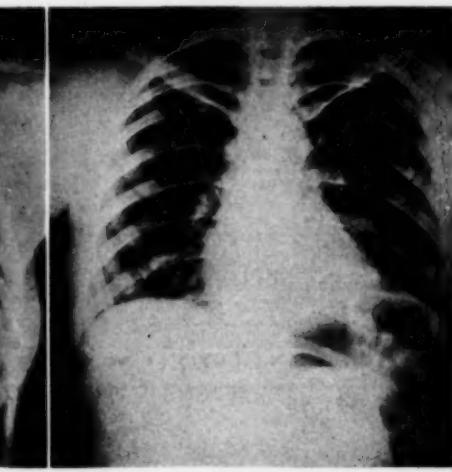
Illus. No. 5, May 1926  
Case No. 15 (Lat)



Illus. No. 6, Jan. 1938  
Case No. 17 (McC)



Illus. No. 7, Nov. 8, 1939  
Case No. 17 (McC)



Illus. No. 8, Feb. 5, 1940  
Case No. 19 (Oli)

point of view, that she exhibited obvious resentment. She was promptly referred to the alternate clinician, who soft-heartedly agreed to two months—the fourth compromise. (Both of these clinicians had daughters of their own). Returning to duty early in Feb. 1941 x-ray film was still clear. A month later, early in March, an enlarged painless axillary gland was noticed. Taken out in April 1941 it was found to be tuberculous. This was 26 months after our first warning. Fault: failure to procure the bed rest indicated for the nurse.

Herewith graph of Case 18 labelled (Man), plainly depicts 26 months' warning of the approach of clinical tuberculosis. Positive Inhibitives, positive Fixations, repeated definite movement in both graphs, and increased tuberculin sensitivity are shown. The rest periods taken were all short of the prescriptions duly considered necessary, even the last period being interfered with by the house taking fire. (See Fig. 11 Graph, Case 18).

During the second year of the above noted period, one of our more recent collaborators had been incidentally watching this work. At the culmination, he commented that he had "had no idea tuberculous disease could be predicted with such precision." Caulfeild said that "all our colleagues who have had adequate and intimate knowledge furnished through the use of the dual serial tests have come to rely upon them."<sup>4</sup> In other words *no one who has set out to acquire such first hand knowledge, over a sufficient period of time, (several consecutive years), has failed to gain confidence in the tests.* "How could the prediction of a disease by a biological test be proved or disproved in less time, when the average incubation period of that disease is three to five years?"<sup>13</sup>

Case 19 (Oli): On entering the school Sept. 1939, was negative to 10 mg. tuberculin, with negative serology and clear x-ray. In Jan. 1940, 1/20 mg. tuberculin gave a positive, and the Inhibitive and Fixation were positive. Serology was then repeated monthly. The Fixation remained positive but stationary, and we have thought that this, *per se*, does not presage danger. The Inhibitive also remained positive and stationary, which we knew was precarious. To those close by, we may have been evincing temporary loss of faith, because we postponed action from month to month, pretending to be content with more frequent tests and x-ray films. In June, the latter showed pleural effusion and a minimal parenchymal lesion. Graph and chest pictures shown below.

Fault: Not wanting to interrupt the nurse's probation, we tarried too long in ordering the required rest, that is, we failed to heed repeated serological warnings. Also, we were apparently dealing with the onset of a primary-infection-type, with its possibly shorter incubation period. (See Fig. 12 Graph, also Illustrations 8, 9 and 10, chest films, Case 19).

Case 20 (H.B.): Case of a preliminary student commencing her training found negative to 1/20 mg. tuberculin, negative to 1 mg., positive (20 x 15 mm.) to 10 mg., negative x-ray film, but with positive C.I. and T.C.F. She was advised to retire from her class, to come back into the next class, taking 3 months' bed rest meanwhile. She begged to be allowed to get her probation first, and we mistakenly acquiesced, perhaps relying somewhat on the fact that the sensitivity to tuberculin was so slight. Ten months later our conscience caused us to write the order for one months' bed rest at home, remarking that we feared we might be too late. At this time, Dec. 4, 1939, 1/20 mg. tuberculin still gave a negative (1 x 1 mm., or needle puncture only), 1 mg. gave 5 x 7 mm.

with induration; 5 mg. gave 8 x 10 mm. induration and 20 x 15 areola, and the x-ray was clear. After return to duty, the x-ray film Feb. 7, 1940 showed a definite minimal parenchymal lesion measuring 8 x 7 mm. on the original 14" x 17" film, situated between the 1st and 2nd left ribs anteriorly, in the lower half of the interspace, in the peripheral zone just inside the inner edge of the scapula, and constituting a density of 20 per cent opacity comparable to that of the anterior portion of a rib close to the sternum. Chest films reproduced herewith. She was then positive to 1/20 mg. tuberculin. On admission to the school, serology had suggested the approach of tuberculous disease in spite of a negative reaction to both 1/20 and 1 mg. tuberculin.

It was this case which taught us that one or even two months might not be sufficient bed-rest to forestall development of demonstrable disease, if the serological graph had been precarious long enough to intimate that disease was likely to be imminent. We therefore, added a prescription for two and also one for three months bed rest. Fault: leniency. (See Illustrations 11 and 12, chest films, Case 20).

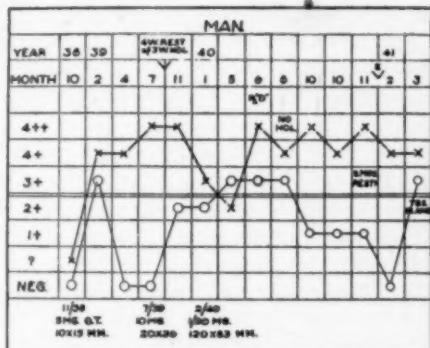


Fig. No. 11, Graph  
Case No. 18 (Man)

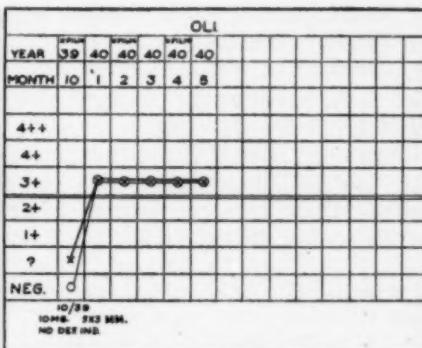
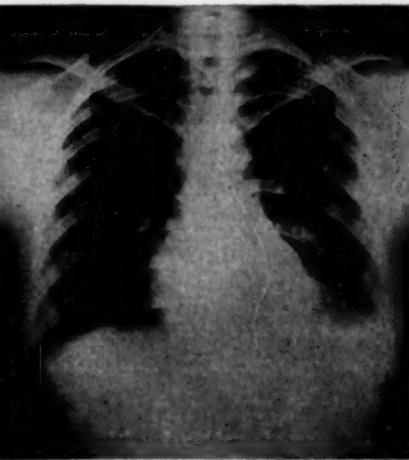


Fig. No. 12, Graph  
Case No. 19 (Oli)



Illus. No. 9, April 23, 1940  
Case No. 19 (Oli)



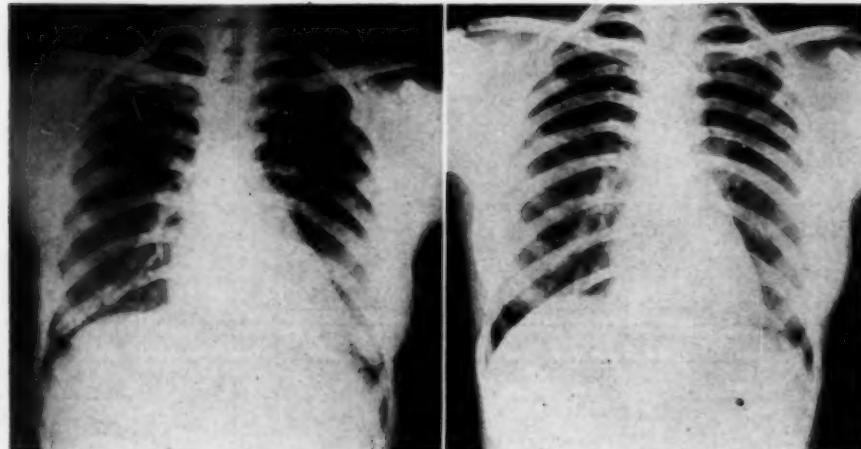
Illus. No. 10, June 2, 1940  
Case No. 19 (Oli)

**Case 21 (T.P.):** Entered the school Sept. 1937 with no reaction to 10 mg. tuberculin and no significant serological reaction. In Dec. 1938 there was a 12 x 8 mm. pink and indurated reaction to 1 mg. tuberculin. In Oct. 1939 C.I. was 2 plus; this, with the previous increase in tuberculin sensitivity made two D.S.P.'s. In Feb. 1940 the T.C.F. moved 2 spaces to 4 plus; in March 1940 there was a 100 x 65 mm. light pink areola and 22 x 18 mm. deep pink markedly indurated reaction to 1/20 mg. tuberculin. Next month April 1940, C.I. was 3 plus, making the 4th D.S.P., and the x-ray film demonstrated a definite lesion.

**Situations for Solution:** Several months prior to this last date, when we advised the nurse that a rest period was needed, it was learned that her home was in Newfoundland, 1,200 miles away, and no funds available to take her there. Enquiries failed to find facilities for the complete rest required. Finally, three months' bed rest in a sanatorium as a 'tuberculosis suspect' was applied for by us and refused by the government authorities.\* Governments cannot spend money for prevention of disease in healthy individuals on the basis of hypotheses not generally accepted. Provision of preventorium care for a child, away from an infectious mother, is to date, more easily understood. When the lesion in the above case became demonstrable in April 1940, we called our administrative friends, and, asking if they recalled our previous request for a bed to prevent tuberculosis, now demanded a bed for actual disease. A free exchange of opinions, theories and facts then took place, but the bed was granted.

Aside from the difficult contingency of long distance from home, exemplified in the case just related, we have had only one other, of comparable difficulty, viz., where disturbing economic or domestic problems prevail in the home, making provision for bed rest out of the question.

\*If specialists apply for admission of a 'tuberculosis suspect' to sanatorium it is assumed that every test and examination has been done and that the case cannot be definitely diagnosed as tuberculous disease. We therefore, in jest, accused the authorities of penalizing us because we were specialists. On the other hand if we had been general practitioners, they would have granted our request, assuming it likely that disease was already present.



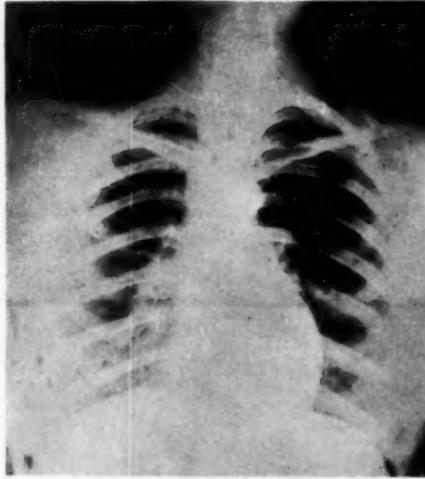
Illus. No. 11, Dec. 4, 1939  
Case No. 20 (HB)

Illus. No. 12, Feb. 7, 1940  
Case No. 20 (HB)

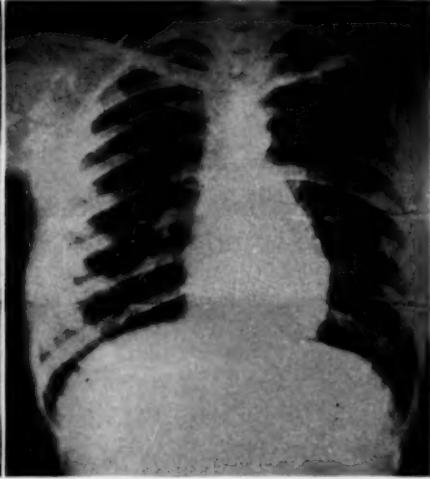
Case 22 (O.D., Mrs. Cas): Husband diagnosed Moderately advanced, April 1931 and went to sanatorium. During the next three years there were five danger signals on our fourth revised clinical interpretation graph, two positives, in addition to three moves of two spaces each. (From this case we learned, that a moving graph may be as significant as positive tests, or more so). No extra rest was taken. Films were clear Dec. 1931, and in Nov. 1933. In May 1934, gross lesion was shown toward right base, and tubercle bacilli found. (See Illustrations 13, 14 and 15, chest films, Case 22).

Case 23 (R.E.): On admission to the school Jan. 1934, was negative to 1 mg. tuberculin, gave  $6 \times 6$  mm. pink induration to 5 mg., and negative Inhibitive and Fixation. In three years, only six serological tests were done instead of the prescribed twelve. Four of the intervals were 8, 10, 6 and 11 months successively, instead of the prescribed maximum of four months. A Danger Signal was shown in Nov. 1935, viz., a move of 2 spaces in the Fixation graph, but at that time we were not aware that such a single move could be a Danger Signal. Then also, tuberculin tests were not repeated every 4 months as now (nor even annually) if the reaction was positive to any one strength. The next tuberculin test was early in 1937 when 1/20 mg. gave  $7 \times 8$  mm. induration and  $15 \times 20$  mm. areola, constituting a second D.S. The nurse left the hospital on graduating, for a year's course elsewhere, and returned in Sept. 1938 with a lesion demonstrable by x-ray. We believe that had serology and tuberculin testing been done every 4 months, sufficient warning of approaching disease would have been given and recognized, to have invoked extra rest and so to have precluded clinical disease. We also feel that the nurse herself might have sensed concern on our part, and have asked whether or not further testing was advisable. The episode cost the nurse three years' rest, mostly in Freeport Sanatorium, and bilateral pneumothorax. She is now on duty at that institution.

Case 24 (H.M.B.): When about to finish training Jan. 1939, there were noted two Danger Signals in this nurse's serological graph, viz., a move



Illus. No. 13, Dec. 1931  
Case No. 22 (Cas)

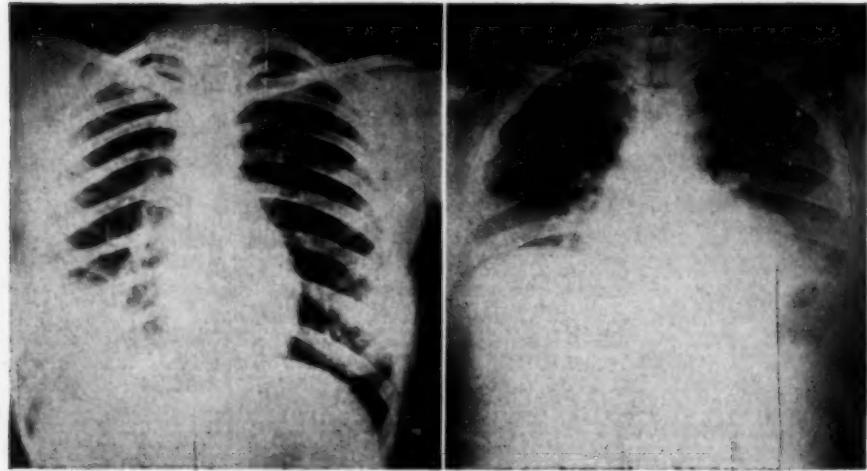


Illus. No. 14, Nov. 1933  
Case No. 22 (Cas)

of two spaces in both C.I. and T.C.F. In June 1937, 1/20 mg. tuberculin had given a definitely positive reaction. Also it was noted that only 3 dual tests had been done in the three years, with intervals of 10 and 8 months, whereas the minimal number considered necessary to give sufficient warning of approaching disease is twelve tests, that is one every 4 months. Much can happen in regard to tuberculosis in 8 or 10 months. Conceivably, if the full quota of tests had been done, there might have been 4 or 6 D.S.P.'s. At this point our staff nurse asked the graduating pupil if she desired the serological observations continued. (Graduates are required to pay a nominal fee of five dollars per year). The answer "No" was written by the staff nurse on the graph sheet. Two years later in Feb. 1941, this nurse became acutely ill with pleural and peritoneal effusion and temperature of 104° F. (The Inhibitive had moved up 4 spaces and the Fixation down 2 spaces, see Rule No. 2). We feel that this could have been anticipated and prevented if the testing had been continued regularly.

Later, in Nov. 1941 in sanatorium, the serology in this nurse's case showed neither test higher than 1 plus, and when on increasing exercise, they remained down for four successive months, she was allowed to leave sanatorium in Feb. 1942. Because of the acute and serious illness at the onset of this case, we withheld permission for full day work for another two months. The nurse has continued on full day duty to date of writing, and the tests are still down and negative. We may have been overly cautious here.

In most of our pleural effusion cases without parenchymal involvement both serological tests have become normal-negative after 4 to 8 months' bed rest and we have then allowed return to work within the year. Likewise with our smaller number of cases of (apparently) localized tuberculous adenitis, where the glands have been excised. (This is in contrast to parenchymal lesions usually requiring a year or more). One of the latter (tuberculous adenitis) was Case 18 (Man), given above, who was sent to Freeport Sanatorium April 1, 1941. When C.I. showed a drop from 3 plus in March 1941 to below 1 plus in Sept. 1941, and when it remained close to the negative line through five successive months,



Illus. No. 15, May 1934  
Case No. 22 (Cas)

Illus. No. 16, March 1926  
Case No. 26 (HCC)

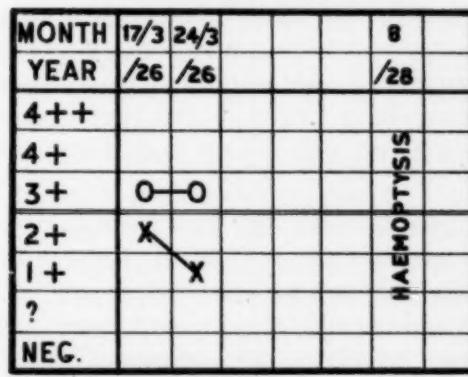
in spite of added exercise, we deduced that tuberculosis as a potential clinical factor had faded out and she was allowed to return to the School, after only 10 months' bed rest, to finish her training. This nurse is on duty to-day.

Case 25 (W.S.): Was the other example of adenitis occurring in the School for Nurses. On admission to the school Sept. 1938, tuberculin 1/20 mg., C.I. and T.C.F. were all negative, while 1 mg. tuberculin gave 35 x 23 mm. over 5 x 7 induration. In Jan. 1939 C.I. gave 2 plus which in the original true laboratory terminology was "indifferent or negative inhibitive." This occurs very rarely in the adult, but seems invariably to forebode evil. We overlooked this Danger Signal. The next blood test was not done for 6 months, and the next tuberculin test for 10 months when the latter was positive to 1/20 mg. This made a second Danger Signal, and still no warning was taken. Three months later in Feb. 1940, an enlarged axillary gland was excised and on examination was found to be tuberculous.

At this point a year's bed rest was prescribed, and as usual, we were asked if there was any possibility of our allowing her to return to duty within the year. We replied, "Only if the blood tests return to normal, and with increasing exercise remain so for several months." A specimen was carefully brought in 100 miles each month. In Sept. 1940, both serological tests had come down. After two successively normal tests, the family physician was advised to prescribe increasing exercise. With the 3rd and 4th monthly tests normal, the nurse returned to duty within the year, finished her course and has remained well. She is now on duty as an Army Nursing Sister.

In the same manner, it has seemed to some of us that we can more readily be informed of the presence of occult or "surgical" tuberculosis, e.g. glands, bones, etc., and also of its abatement or "cure," than we can in pulmonary tuberculosis. This was recently mentioned by one of us<sup>13</sup> and fifteen years earlier by another of us (H.M.), when he used serology in deciding in what year and month, termination of bed rest in vertebral and glandular tuberculosis could safely be permitted.

NAME C.H. (WIFE TUBERCULOUS 1924)



O—O = INHIBITIVE  
X—X = FIXATION

Fig. No. 13, Graph  
Case No. 26 (HCC)

Case 26 (H.C.C.): Active minimal pulmonary tuberculosis was diagnosed in the wife of a physician, Dec. 1924, and she went to sanatorium. The husband was serologically tested March 1926 as a contact, although he protested that infection was impossible in the absence of any expectoration, cough or clearing of the throat by the wife. The Inhibitive was positive and the husband was warned, whereupon he reminded us that he, as a laboratory trained physician, and his wife as a graduate in law, were both entitled to unusual credit as to accuracy in making a statement. Finally he asked, "Could not the laboratory be in error in the occasional test?" This we admitted, (Caulfeild and Anglin referred to 2 per cent "false positives" in the Inhibitive and 13 per cent "false positives" in the Fixation)<sup>4</sup> and therefore repeated the test the following week, again obtaining positive Inhibitive. We then more strongly admonished him to restrict the expenditure of his energies, and he in return thumbed his nose, this time because he weighed 180 lbs. and his x-ray film was clear. Twenty-nine months later, in August 1928, at 220 lbs., he had a frank hemoptysis, and x-ray film showed parenchymal involvement over the right second and third anterior inter-spaces, this being forty-four months after contact was broken. It required 10 months to resolve. Graph and chest pictures shown herewith. (See Fig 13 Graph, and Illustrations 16 and 17, chest films, Case 26).

#### RE POSSIBLE FALSE POSITIVES

The above is cited chiefly to exemplify the procedure in checking a possible "false positive" Inhibitive reaction; the Inhibitive is a very labile reaction. If there has been a laboratory error, it will presumably be corrected when the test is repeated, not in the same week but in the following week. This is so, because a different complement is used every week, that is, from a different guinea pig. It is preferable that the repeat test be not delayed more than a week or two, at least the stress under which the individual works, must not vary, otherwise his physiologic reserve varies, and so in turn will his Inhibitive reaction vary. (See diagram of biological sequences in the development of tuberculous disease). Under such uncertainties it would be difficult to differentiate between a false positive Inhibitive and a true Danger Signal as shown in a changing serologic graph. Two examples of the latter were given in cases No. 5 (Arn) and 6 (Jef); each gave positive Inhibitive before the rest period and negative Inhibitive following the rest period.

The finding of positive serologic reactions in apparently normal persons has been another cause of head-shaking by some of those observing our work. Through a period of twenty years twelve physicians were given serological warning of the probable approach of tuberculous disease. As far as was apparent, none of them gave any heed to this warning. Nine of the twelve were subsequently known to have demonstrable tuberculosis; eight of the nine showed clinically active disease, while in one it was discovered only at

necropsy (Case 27, "M.J." below); one of the nine has since died of tuberculosis. "With a precarious graph, biological tuberculous disease undoubtedly obtains; whether clinical tuberculosis soon becomes manifest or be found only at autopsy following a long and useful life depends on the balance between the physiological fatigue and physiological reserve (à la Holman)."<sup>22,23</sup> There are those who seem to forget what they were taught, and what possibly they teach in their own lectures, viz., that in a certain small but definite percentage of cases, *tuberculosis not suspected during life* is found only at autopsy. It has remained for Henry C. Sweany and associates to bring these percentages up to date. Writing under the title "Evidences of Tuberculous Infection in People Dying of Other Causes than Tuberculosis," he says: "Positive cultures were obtained in 16.53 per cent of 212 cases . . . 10.38 per cent showed acid-fast bacilli on smears."<sup>24</sup> This same author kindly permits us to quote his "results in 983 autopsies, on persons dying of other than tuberculosis, where more infants and children are included, in which 114 gave positive cultures, a percentage of 11.59."<sup>25</sup>

The series of a dozen doctors under serological observation, related above, could be taken as a yardstick in estimating the percentage of positive serological reactors who subsequently develop the disease.

Case 27 (M.J., physician): Came to one of us (O) Feb. 1920, concerning a knee which we diagnosed as non-tuberculous, but the patient as potentially tuberculous because of positive Inhibitive. We advised that she take sheltered employment at a sanatorium (Mountain). No tuberculous disease was ever manifest clinically. Demise from a non-tuberculous cause in 1930 was followed by necropsy, which revealed long-standing lymphatic tuberculosis. A phthisiologist and friend then wrote acknowledging aroused interest in serology. We thanked him, but asked, was it not strange that some of us had to await postmortem on a friend before taking notice of new tests?

Referring again to Caulfeild and Anglin's published percentages of so-called "false positive" serological tests in tuberculin negative normals, we must point out that they used tuberculin only up to  $\frac{1}{2}$  mg. Case No. 20 (H.B.) above, giving positive C.I. and T.C.F., and negative to 1 mg. O.T., positive only to 10 mg. on admission, and developing tuberculous disease in ten months, has helped to convince us that we can be guided more safely by including the use of 10 mg. tuberculin. It also suggests that with such dosage, "false positive" serologic reactions in tuberculin negative normals may constitute an even smaller percentage.

#### TUBERCULIN TESTING

Five years ago we analysed the records of two score of nurses and contacts who had developed tuberculosis under observation,

looking for possible missing factors which might have given us additional information in regard to the onset of the disease. The commonest factor was the *absence of recent tuberculin tests*. When the disease was discovered and the tuberculin test then repeated, sensitivity was present where it had not been previously, and in others it had markedly increased. Since then, we have set out to retest nurses with tuberculin every four months whether they have shown sensitivity to any of the three dilutions or to none. The only ones we do not usually repeat, are those already markedly sensitive to 1/20 mg., e.g. giving an areola say of 100 mm. diameters with central vesiculation. The next missing factor was *regularity* in serological testing. The third factor was *lack of strictness* on our part, or *quiet evasion* of instructions (for rest) on the part of the nurse or contact.

Tuberculin reactions are given in precise figures, shades of color, induration, and possible vesiculation, in preference to the loose terminology "negative, one plus or two plus," commonly used. This is because we believe that if the phthisiologist himself cannot see the site of the injection in from 24 to 48 hours, he should be given as exact a reading as possible, and be allowed to make his own interpretation, whether there is or is not a reaction, and if present, whether due to tuberculin or trauma. D. W. Crombie of Queen Alexandra Sanatorium, London, Ontario, has commented that a definite pink area 3 by 3 mm. in size, should not necessarily be read as negative "particularly if there is any induration."<sup>26</sup> The trauma commonly produced by a number 26 needle measures 3 by 2 mm. Slight induration or oedema is most easily recognized by *lightly* drawing the little finger across the site.

There is yet another procedure which we believe could be improved upon, viz. the time elapsing between the intracutaneous injection of the tuberculin and the reading of any reaction. We think there is frequently a true though evanescent reaction to be seen at 24 or 36 hours and not at 48 hours. Dr. Donald T. Fraser and Dr. Frieda Fraser of the Connaught Laboratories, Toronto add<sup>27</sup> "that one may see such early reactions in persons who, when tested with a higher dose of tuberculin do *not* give any increased reaction and should on that basis not be considered positive. In other words, a suspicious positive does not always reveal itself as a definite positive when tested with a higher dose of tuberculin." Our chest clinic is held only twice weekly, one in the late afternoon and the other in the morning. In such circumstances reactions are read at two and one-half day or four and one-half day intervals. For more correct interpretation we ourselves should read them at both 24 and 48 hour intervals, or train a nurse to do so. The possibility of a delayed reaction at 72

hours should not be overlooked. J. A. Meyers in his text-book said<sup>28</sup> "tuberculin reaction is read in 12 to 48 hours."

We hold as did Caulfeild that tuberculin testing gives relative rather than 100 per cent positive information.

Some of us have been tuberculin testing our children semi-annually with a view to having information at an early date of acquired tuberculous infection. Thereupon, somewhat greater physiologic rest might conceivably forestall the development of tuberculous disease. At this point in the tracing of tuberculous infection, it is known that a certain small percentage develop disease from year to year following infection. Therefore a few of us, with serological testing available, adopted its periodic use in these children, following the finding that they had been infected, in order to differentiate between those who are liable to develop disease and those who are not. We need then apply restrictions only to the small percentage showing danger in their serological graphs.

In this particular phase of tuberculosis prevention work, the crash of Case 28 (S.R.) described below, into acute pleural effusion within five months of being negative to 10 mg. tuberculin, brought vividly before us an unpleasant possibility. It could happen that one of our medical friends, whose children we had been tuberculin testing on the 6 months interval, would call us by telephone four or five months after a negative tuberculin test, and inform us that Johnnie's chest was half full of fluid. To offset this possibility of development of a full blown primary-infection-type tuberculosis without warning, it would therefore seem necessary to carry out tests at least every two months, using the three successive strengths of tuberculin, and a fourth office call to read the third test, thus requiring 24 short office visits yearly. Leaving out of consideration for the present the (more elusive) primary-infection-type just mentioned, an office practice can carry one to two hundred contacts and normals, with tuberculin testing or serological tests or both, with little additional time and effort. For this type of practice we have employed the designation "periodic testing of normals (P.T.O.N.)."

So, in a nursing school with 10 pupils (in a class of 50), negative to 10 mg. tuberculin on admission, the number of interviews (tuberculin testing or reading) would be 40 bimonthly or 240 yearly, all with the purpose of learning when infection has taken place and when to commence serological tests. We have yet to learn whether it be possible to anticipate in time, and totally prevent, all primary-infection-type tuberculosis. With our tuberculin routine outlined above, when a positive is first found, it may be necessary to test serologically every two weeks, at least until the graph is found

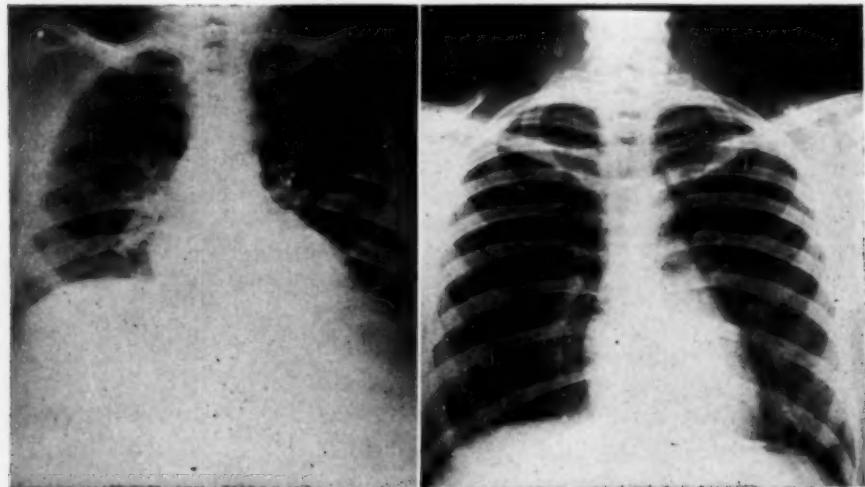
steady, or until several Danger Signs cause us to prescribe an immediate rest.

In private practice, one may well hesitate in offering 100 per cent ensurance against primary-infection-type (childhood) tuberculosis, as it requires at least 24 appointments per year, up to the time when a positive tuberculin test may occur. Even then we have some doubt whether we could expect to obtain sufficient warning from serology within the possible short four months incubation period of this type; it may prove quicker "on the draw" than we. Compared to the above, *the foreseeing and forestalling of the reinfection-type (adult) tuberculosis is easy*, with its much longer latent or incubation period, which provides ample time, not only to get warning from serology, but also sufficient time to apply the additional rest needed to prevent the development of actual disease. The only possible failure would be where, in the entire absence of hygiene, an individual might ingest such excessive or massive doses of tubercle bacilli, as no amount of physiologic reserve could master.

#### MORE ABOUT TUBERCULIN TESTING, WITH EXAMPLES

**Case 28 (S.R.):** There recently developed in Aug. 1943, pleural effusion in one of our nurses who was negative to 10 mg. tuberculin in March. Repeated Aug. 1943 by one of us (H.I.K.), she gave a marked reaction (40 x 30 mm. areola and 15 x 12 mm. red induration) to 1/20 mg. (See Illustrations 18 and 19, chest films, Case 28).

This case represents the primary-infection-type of tuberculosis, the one type about whose prevention we have not been so sanguine. In the commonest type of disabling tuberculous disease, viz. the



Illus. No. 17, Aug. 1928  
Case No. 26 (HCC)

Illus. No. 18, Dec. 1942  
Case No. 28 (S. R.)

reinfection-type, we get warnings by immunological reactions of the patient's serum during 6 to 24 months of an incubation period of unusual length, affording us ample time to raise his defences by extra rest. What chance have we, however, in the primary-infection-type where the tissue permeability to the bacillus can apparently be much greater and where the incubation period can be under six months? The last two previous cases which we had, of this primary-infection-type, were hilar lesions shown by x-ray, taken when semi-annual tuberculin tests became positive (the last examples published recently by one of us<sup>13</sup>). It was chiefly this type which prompted us to increase the frequency of tuberculin testing from every 6 to 4 months. If this most recent case, S.R., given above, had had her regular four-monthly tuberculin test in July, when it was due, it would presumably have been positive. Would it have been possible, even if prompt bed rest had been taken, to forestall the development of clinical disease the following month? This being doubtful, all nurses negative to 10 mg. tuberculin are now retested every 2 months. (This case, S.R. died in six months with meningeal symptoms).

The above reasoning and change in procedure again indicates our quest, viz. the search for the earliest possible warning signal, in which the organisms, by an allergic or immunological reaction, tells us that it is reacting to an attack by tubercle bacilli. In following possible contacts, it has not been our custom to test serologically until they are positive to 1/20 mg. or to 1 mg. tuberculin. With the nurses however, from the beginning of the work and survey, we have tested all serologically, whether giving any reaction to tuberculin or not. (Note case 20, H.B. above, which gave two serological warnings when reacting only to 10 mg.). We would like to know which may give the earliest indication of attack by the tubercle bacillus, tuberculin or serology. Mention may be made here of a preliminary finding in some laboratory work with animals, by one of us (M.F. MacL), with this question in mind. In quite a small series of four guinea pigs, Fixation was positive in five weeks. Inhibitive showed a *tendency* toward Inhibitive reaction in nine weeks but as sera were anti-complementary on this date readings were not reliable. Positive Inhibitive reactions were not obtained in any test of this series.

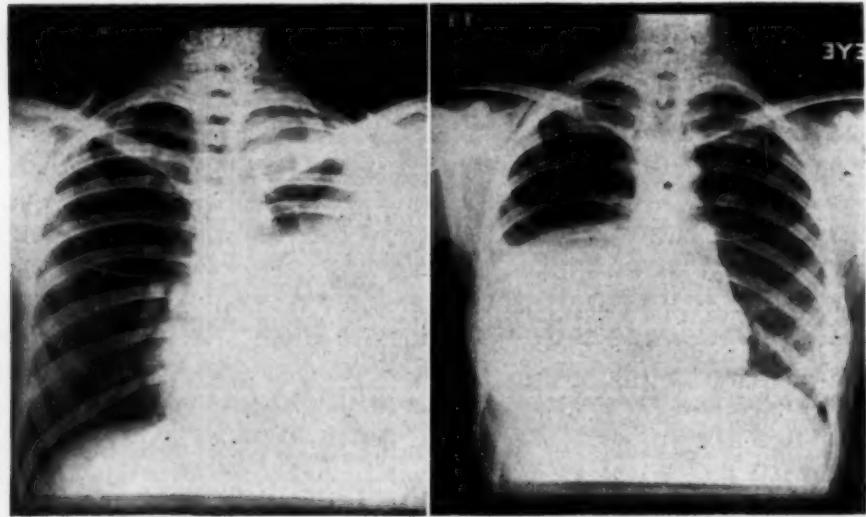
In the use of 3 tuberculin dilutions instead of one or two, we feel that we have a distinct advantage. If a nurse has received her first or fresh tuberculous infection as recently as 3 or 4 weeks previously, we will get a reaction to the 10 mg. dose where we may not to the 1/20 or the 1 mg. If in this case she reacts to the 10 mg. for the first time, but not to the 1 mg., the tests are repeated in 2 to 4 weeks. If then positive to 1 mg. but not to 1/20, these are

repeated in another fortnight or month. If now she is sensitive to 1/20 mg., appeal to serology is at once made, and if the answers are indecisive, the tests are repeated at monthly or shorter intervals.

**Case 29 (Y.M.):** Here follows an example in which the logic of our convictions given in the paragraph immediately above, was not followed, with unfortunate consequence. "Of what use is 10 mgs. tuberculin? What danger is there in two hours' exposure among intelligent and hygienic folk? Why alarm people unnecessarily?"

A girl of 22 reported because her best friend, girl, also 22, had been diagnosed tuberculous the previous month with positive sputum and cough. They had been *together only two hours in each week*. The contact was tested intradermally Feb. 8th with 1/20 mg. tuberculin. Seen Feb. 9th there was only a 1 x 1 mm. mark, and 1 mg. was given. On Feb. 10th, only 1 x 1 mm. mark was visible and 10 mg. was used. Next day, Feb. 11th, a faint pink areola of 20 x 15 mm. was seen, with slight palpable induration. The two previous tests still showed no reaction. How slight any indication of infection! True, if infection had taken place in the previous two or three weeks, the 10 mg. dose would be the only one that could show it. But exposure must have been only in the most recent two, four or six hours during which they were together; if it had been for 10 or 20 hours, some must have occurred five to ten weeks previously, and then the 1/20 or the 1 mg. would have shown it. We compromised by giving an appointment for three months later.

On May 10th, 1/20 mg. was given intracutaneously, and the next day, May 11th, there was a dull pink areola of 35 x 22 mm. with induration plus. We now enquired as to hours of work and rest. She was private secretary to the manager of a large business, her rising hour was 7:30, her average lights-out hour 12:30, except twice weekly when it was 1:30. We considered it advisable to advance the average lights-out hour to 10:30, and were informed this was not possible because she was "too



ILLUS. NO. 19, AUG. 1943  
Case No. 28 (S.R.)

ILLUS. NO. 20, JUNE  
Case No. 29 (Y.M.)

full of pep." A month later pleural friction was heard (HIK), and two weeks later still, pleural effusion demonstrated (ELS), as seen in chest film reproduced herewith. Our deductions from the use of 10 mg. tuberculin in February should have been followed up by retesting with tuberculin in March. We would have had our information two months earlier. (See Illustration 20, chest film, Case 29).

If our objective is only case finding, of ever-so-early and minimal cases, firstly to shorten the cure for the same, and secondly by segregation and arrest of the disease, to prevent them becoming spreaders of the infection, then the higher doses of tuberculin, 1 mg. and 10 mg. have little place in our armamentarium. The only place for the 1 mg. dosage in survey work is in greater accuracy as to tuberculin sensitivity where it is not possible to read reactions at 24, 48 and 72 hour intervals, e.g., if a reaction at 48 hours is a questionable pink or induration, the answer can usually be obtained by giving 1 mg. and reading it 48 hours later. *If however, our objective is the anticipation and actual prevention of all tuberculous disease*, then the 1 and 10 mg. tuberculin dosage is necessary, in correlation with studies of the blood serum.

#### DEFINITION OF A CONTACT, AND QUESTIONNAIRE RE EXPOSURE

When we commenced, in 1920, at the suggestion of Caulfeild, the following of contacts with the use of serological tests, it was our confidence in their specificity for tuberculosis that set us scrutinizing the history of exposure as first given. One in every four or five referred to clinic or office as contacts, were found to give repeatedly negative serological tests, and occasionally, negative tuberculin tests. It was therefore decided that a more specific definition for "contact" should be attempted, and a more methodical scheme of questioning should be evolved, for the purpose of eliminating those not actually exposed. The definition given at that time read as follows: "All contact-cases were known to have associated with a tuberculous patient who had tubercle bacilli in the sputum. 'Associated with' means more than a total of a dozen hours in the same unventilated room, with the disease present, but as yet undiagnosed, and the patient untrained. Casual meeting out of doors or visiting on an open verandah is not counted as contact." We admit that the number of hours specified, namely a "dozen," was entirely arbitrary. It is nevertheless of interest, although merely coincidental, that the number of hours of assumed exposure in the Case 29 (Y.M.), just related, is just half a "dozen". The case was assumed to be of the "primary-infection-type".

It has been our observation over a number of years that acceptably exact and correct histories of exposure to tuberculous infec-

tion, in the total number of hours, with dates, are very rarely obtained. They may occur only in one per cent of our cases. It should therefore be of interest to add three more exceptionally accurate histories of exposure, all of the reinfection type.

**Case 30 (Ny):** Admitted to a ward by one of us (G.C.A.) from O.P.D., T.W.H., Oct. 1934, with minimal parenchymal lesion on one side and pleural effusion on the other. Her husband had left her in 1924. In 1926 he was in penitentiary. In 1931 he appeared at her door, ill. She took him in, put him in her own bed, nursed him, obtained medical attention and a diagnosis of advanced pulmonary tuberculosis was made, with positive sputum. At the end of seven days, he was removed to sanatorium. Thirty months after this she came to the Toronto Western Hospital, O.D., as stated above. The intimate exposure in this case was ten hours per day for seven days, totalling seventy hours. As we are discussing at the moment only histories with precise and accurate dates and number of hours exposure, it may be worth commenting here, that this seventy hours is the shortest exposure of which we have record, that logically seemed to have resulted in a lesion. We note that at 45 years of age, this case can be assumed to be the reinfection-type. Note also the incubation or latent period of thirty months in relation to the comparatively short exposure.

**Case 31 (Chun):** In contrast to the case just related, this Chinese had a much longer intimate exposure and (logically, we think) a much shorter incubation period. He was diagnosed by one of us (E.L.S.) with the late Harold Parsons, Nov. 30th, 1934, in the T.G.H., O.P.D., Chest Clinic, as bi-lateral minimal parenchymal tuberculosis. He had been brought to the clinic by the City D.P.H. because a close associate at work had been admitted to a T.G.H. ward on October 30, 1934, with far advanced pulmonary tuberculosis, cough and positive sputum, and had died on November 17th. The new case or "contact," and the infector or so-called "source," had come together for the first time, August 1st of the same year, to work in a laundry. They had been in the same room within ten feet of each other, for twelve hours a day, throughout the months of August, September and October, making just over a thousand hours exposure in the ninety days. This is the shortest incubation period of an assumed reinfection-type, of which we have record, and is to be noted in relation to the comparatively long and heavy exposure.

It may be supposed that in civilized communities, where hygiene and care are taught, that seldom is such heavy or massive dosage of tuberculous infection received, that it becomes the deciding factor, and within comparatively few months terminates the case, no matter what treatment is given. Logically, however, it must occasionally happen. This last idea may not be left unqualified. Hill states: "What really matters as to the final outcome is the size to which, by fission, the dose of infection, be it initially 'large' or 'small,' may ultimately grow."<sup>29</sup> We do feel, however, that the relative size of dosage of infection is the most important factor governing the length of incubation period; the larger the dosage,

the shorter the incubation period, and vice versa. Physiological fatigue is the second largest factor in the development of tuberculous infection into disease, and in controlling the length of the incubation period.

We have a third reasonably accurate history of exposure, Case 32 (B.C.) which in its particular details, seems logically to fill the requirements for certain death, mentioned in the first half of the last paragraph. A mother (O.D. 69731) related part of the history by saying that her son Bill followed her a month later, into sanatorium, as a minimal case with "no" symptoms, but in a few weeks became ill, and steadily failed, in spite of best care, until he died in a year's time. We enquired, and learned of no complications that might explain the rapid failure and death, but the mother kept the subject before us, by offering only two possible alternate explanations, viz., either the doctor who sent him to the sanatorium diagnosed the case minimal, when it was advanced, or the sanatorium doctors did not properly treat a minimal case.

As we repeatedly enquired into the history of "Bill's" case, another son related circumstances which persuaded us that Bill probably received an uncontrollable dosage of tubercle bacilli. All through the previous winter, the mother and Bill shared a three-roomed apartment. The mother had such a bad "bronchitis" and cough, that the windows were never open, and the place was so hot that when the other son and the daughter visited, they felt suffocated. The mother went to sanatorium in May, an advanced case with positive sputum, and son Bill in June. Six months from November to May inclusive, at say 12 hours in every 24, totalling over 2000 hours exposure of assumed unusually saturated and undiluted atmosphere, could well provide the lethal dose. "The mere massive onslaught of large doses of bacteria, as so often used in experiments may undoubtedly break down our defenses, but such, in the natural history of infection, only occurs under the rarest conditions."<sup>23</sup>

The above series of observations led us in 1935, to question the assumed disparity in the inherent resistance to tuberculosis, between the red, black, yellow and white races and to feel that hygiene or lack of hygiene, play more important parts.

In our lectures to nurses we are accustomed to recall to them the procedure followed on entering a garage in a motor car. If the garage is large, and if the garage doors are open, the engine may not be turned off. If, however, the garage is small and the garage doors closed, someone will see that the engine is shut off. Dilution of the poisonous carbon monoxide in the large garage with the open doors is relied upon. Just so, we advise, if they cannot control the patient's cough, they at least can dilute the atmos-

phere about the bed where they are working, by seeing to it that there is a crossward ventilation, by the careful use of windows.

With all this, therefore, ample need is seen for a more explicit questionnaire than is in general use. This follows herewith, taken from our T.W.H. O.D. Chest Clinic Chart of the past ten years. The valuable information, "over what period of time were tubercle bacilli present in the expectoration," is almost never available. The answer is sought in questions 10 and 11 of column one.

#### QUESTIONNAIRE RE EXPOSURE

If more than one possible infector, label answers "A yes, B no"

##### *History of Infector or Possible Source of Infection*

1. Name \_\_\_\_\_
2. Was tuberculosis definitely diagnosed? \_\_\_\_\_
3. When? \_\_\_\_\_
4. How? \_\_\_\_\_
5. By whom? \_\_\_\_\_
6. Lungs, or, and \_\_\_\_\_
7. Had (s)he a cough? \_\_\_\_\_
8. For \_\_\_\_\_ weeks, \_\_\_\_\_ months, \_\_\_\_\_ years.
9. Had (s)he any phlegm? \_\_\_\_\_
10. Were tuberculosis germs found? \_\_\_\_\_
11. When first found? \_\_\_\_\_
12. Had infector been sanatorium trained before exposure? \_\_\_\_\_
13. Was mouth covered by handkerchief (not hand) when coughing, and was sputum destroyed? \_\_\_\_\_
14. How long ailing? \_\_\_\_\_
15. Did (s)he die of tuberculosis? \_\_\_\_\_
16. When? \_\_\_\_\_

##### *History of the Contact or Person Exposed*

1. Relationship to infector \_\_\_\_\_
2. Living, working, eating or visiting together \_\_\_\_\_
3. Same bed, room, table, workshop or house \_\_\_\_\_
4. If workshop, 5, 10 or 20 feet away? \_\_\_\_\_
5. Daily, weekly or monthly frequency \_\_\_\_\_
6. How long at a time? \_\_\_\_\_
7. Over what period? \_\_\_\_\_
8. Beginning of that period \_\_\_\_\_
9. End of that period \_\_\_\_\_
10. Approximate number of hours in same room, e.g., 2 hours in an evening twice weekly for 6 months makes  $2 \times 2 \times 25$  weeks = 100 hours intimate exposure \_\_\_\_\_
11. Windows usually open or closed \_\_\_\_\_
12. Does interrogator consider infection likely? \_\_\_\_\_

Applying the precise stipulations enumerated in these several pages, we carefully scrutinized the previous histories of possible exposure of every new case coming before us, over a fifteen year period, in two large general hospital chest clinics (one of 3,000 and the other of 6,000 annual attendances), and in a sanatorium of 150 beds. It had seemed to us, in 1929<sup>3</sup> that the average time between intimate exposure and the development of a lesion was three years. Our later reckoning however, in 1936, in a series of 100 cases (all but a half dozen with clinical manifestations and all with acceptably accurate history of only one intimate exposure), gave an average of over five years as the incubation or latent period. One only, of this hundred, might be classed as the primary-

infection-type having been tested and found negative to 10 mg. tuberculin nine months before a gross lesion was discovered.

If, as intimated previously, a history of exposure, reasonably exact as to dates, hours, intimacy, careless coughing and presence of tubercle bacilli, is only obtainable in about one in every hundred cases, then the total number of histories studied to obtain the above hundred, must have approximated 10,000. Early in the survey it was found that only some twenty to twenty-five per cent of tuberculous patients could tell of a previous intimate exposure.

In less than a half dozen cases was the exposure within the previous twelve months. When our average was five years, then there must have been some latent periods reckoned as over ten or even twenty years. When such seemed to be probable, if our patient had moved about the country and the health of his associates was not known, that case was discarded from count, and so the great majority were excluded from our reckoning, as being uncertain.

At this point another question comes easily to mind. Where the only intimate and gross exposure to tubercle bacilli occurred 10, 15 or 20 years previous to the breakdown, *just what might have finally caused the development of disease* after the infection had remained dormant so long? We think the answer can be found in balancing or weighing the factors stressed by Holman 15 years ago.<sup>23</sup> Here again an actual case history, No. 33 (H.O.) explains itself, when all details and possible factors are enquired for and elicited. A girl of 19 (O.D. 66910) was found February 1942 by chest film to have the area of two interspaces mostly filled with coarse patchy mottling, indicating parenchymal tuberculosis. Film of two years previously showed none. The mother had been diagnosed advanced pulmonary tuberculous with positive sputum in April 1931, had gone to sanatorium, and died there September 1939. The daughter was under periodic observation at the Hospital O.P.D. as a tuberculin-positive contact, and at school until the death of the mother. The girl then, at 16 years of age, took a job of work, and set out also to take some additional responsibility for her brother, two years younger. We feel that these two sentences logically tell the story. As long as she was at school and her mother alive, any physical and mental stress was not undue, and her physiological reserve was sufficient to weigh against her tuberculous infection for eight years. Her mother's death changed all that, and the extra weight of work, and worry over the 14 year old brother, produced *fatigue*, lowered her reserve, and tuberculous disease became manifest at 19, two and one-half years after death of her mother.

Is the above not a very common story? The usual carefree child-

hood, perhaps also carefree teens and even the twenties, gradually or suddenly having to take the world seriously, and in three to ten years going to sanatorium; teen-age girl breaks down following her debutant year; the duty-conscious male head of a family, realizing he has no financial reserves at say fifty, succumbs to tuberculosis in the next five years; or the graduate nurse, infected or reinfected during her hospital training, adds to her appreciation of responsibility by earning her living in the practice of her profession, or by marrying and starting a family, and she then breaks.

"There are so many kinds of fatigue, that our ideas are apt to be too general or too limited. Normally the cells of the body are resistant to bacterial infection and the failure in this resistance is,—a failure to react,—a fatigue in the normal mechanism of defense. We have over-emphasized the dominant position of the microorganism as the exclusive causative agent in the infectious diseases—numerous factors determine the invasion. Under the circumstances of life, there is a far better hope that we may learn how to prevent the fatigue condition of, e.g., the respiratory tract than that we will ever be able to interfere with the spread of (oral) bacteria (from mouth to mouth). The difficulty is to determine what may be the factors inducing fatigue. Sometimes too much, sometimes too little of a special constituent of the diet,—worry and a thousand and one things lead to the lowering of reserve energy. . . ."<sup>23</sup>

**Case 34 (E.M.):** More recently, a nurse-in-training in another school went home to Manitoba for bed rest because of tuberculous pleurisy. The usual prescription of time and stipulations for treatment were given as in Case No. 25 (W.S.) above, and the impossibility was explained of having blood specimens from such distance, 1,500 miles, arrive in good condition at the laboratory within 24 hours of being drawn. This pupil then undertook to employ air express to overcome this difficulty, the specimen being sent packed in ice in a Thermos flask. It had previously been determined that specimens handled in this manner arrived in condition satisfactory for testing, provided that the sera were removed from the clots within twenty-four hours after blood withdrawal. In five successive months the serum arrived in good condition and was withdrawn from the clot within the specified time. Serological tests being normal, and remaining so on increasing exercise, this nurse returned to duty eight months after her attack of pleurisy. She graduated and has been on duty to date with normal negative serological tests, and is quite well.

It is worth recording here that twice monthly through two successive years, each of two separate organizations forwarded by railway express, twenty blood specimens packed in ice in a picnic Thermos flask, and that they arrived at the laboratory within the specified time and in good condition. The distances were sixty and ninety miles. (M.F.M. and D.V.K.).

## COMMENT

We have shown, that by immunological serum reactions during a very long incubation or latent period, we foresee the disease tuberculosis, one or two years ahead, and forestall it by extra rest. Even in preventive medicine this method of approach is new, and a new approach in medicine is given little or no credence by our conventionalist majority. "*On ne l'a jamais fait, c'est impossible!*" Any test or procedure that does not conform to their preconceived idea of the disease or condition, must be wrong, unless it is at once dramatic and self-evident. de Seversky said, "stubborn orthodoxy retarded air power in the U. S." Could such obtain in medicine?

SUMMARY OF COINCIDENTAL FINDINGS  
NOT DIRECTLY RELEVANT TO THE MAIN THEME

(listed in the same order as in the text)

1) If "silent" or symptomless minimal tuberculous lesions, found by routine or mass x-ray survey, are judged to be possibly "arrested" or "apparently cured," and are associated with normal serum reactions, the patient is allowed to remain at work pending further serological study. If the graph of these reactions becomes unfavorable, the individual is disqualified for work and a rest period is advised; if the graph remains favorable, his work is not interrupted.

An example is given of a nurse applying for training, found by routine x-ray to have bilateral apical minimal tuberculous lesions of the parenchyma. Normal blood serum reactions indicated no potential activity and she was admitted to the school. As throughout her training the serological graphs continued favorable, she was permitted to complete her three year course, and the x-ray picture remained "in statu quo".

2) The shortest incubation period observed in a case of pleural effusion, being of the primary infection type, was four months. In March 1943, a twenty-year old girl was negative to 10 mgs. of tuberculin in July 1943, there was pleural effusion. (The meninges became involved and she died January 1944).

3) The shortest intimate exposure which apparently resulted in a case of tuberculous effusion of the primary infection type, was six hours. A twenty-two year old girl was negative to 10 mgs. of tuberculin in January, the exposure was in the same month, and pleural effusion developed in the following June.

4) The 10 mg. dosage in tuberculin testing has definite value, though its place is restricted.

5) "Tuberculosis Contact" is defined. It is also graded by the number of hours of intimate exposure.

- 6) The shortest intimate exposure in the series, resulting in a case of the re-infection type of (pulmonary) tuberculosis  $2\frac{1}{2}$  years later, was seventy hours.
- 7) The shortest incubation period in a case of the re-infection type of pulmonary tuberculosis was four months. The intimate exposure was one thousand hours.
- 8) Lethal or "per se" necessarily fatal dosage of tubercle bacilli (in the re-infection type) is rare in civilized and hygienic communities.
- 9) The greater the intimate exposure and the larger the dosage of tubercle bacilli received, the shorter is the incubation period.
- 10) After infection has taken place, physiological fatigue is seen as the largest factor (second only to a possible massive dosage), in the development of the disease.
- 11) The assumed disparity in the inherent resistance to tuberculosis between the red, black, yellow and white races is questioned; hygienic factors are probably more important than race, in that they influence firstly the dosage of infection, whether it be minimal, gross or massive, and secondly the resistance of the individual.
- 12) The average incubation period in the re-infection type is reckoned as being between four and six years.

#### SUMMARY

- 1) Tuberculosis contacts and nurses-in-training are tested with tuberculin every 4 months. If and when positive, they are then serologically tested every 4 months.
- 2) Danger signs of approaching tuberculous disease are seen when successive Inhibitive or Fixation reactions produce certain positive or significant serological graphs. A graph showing variation portends more imminent danger than if merely positive. It is explained that this is understandable with immunological reactions. Recent marked increase in tuberculin sensitivity adds to the precariousness of the situation.
- 3) When Danger Signs are seen in the graphs of nurses on full-day duty, we order sleep in their daily hours off, and the deletion of four of their six late leaves per month. This usually dissipates the danger, and tuberculous disease fails to develop. If however, the danger does not disappear after several months of this enforced rest, we change the prescription to one, two or three months in bed at home. With contacts on ordinary 7 or 8 hour-a-day work, advancing the average lights-out hour from 12 p. m. to 11 or from 11 to 10 is usually sufficient; alternate week-ends in bed, may be added. Failure in taking the rest results sooner or later in the development of tuberculosis in most of these individuals.

4) Three examples of a safe graph are shown: no danger signals, no extra rest taken, and no tuberculosis developed. Ten examples of danger warning graphs are shown, where extra rest was taken, the danger signals abated, and no disease developed. A dozen danger warning graphs are then shown where the prescribed rest was not taken, and tuberculosis did develop.

5) The two main factors in the success of the method are, firstly, precision in the interpretation of tests, and secondly, firmness in prescribing rest on a purely hypothetical basis and in the absence of symptoms or any manifest abnormality.

#### CONCLUSIONS

With comparatively little expense and a clinical laboratory team interested in preventive medicine, and with full co-operation, there need be no tuberculosis in a community. It should be possible to arrange any community into suitable groups, as to time and place, for convenience of testing, instruction and control. Groups most easily so supervised, are nurses-in-training, and tuberculosis contacts in chest clinics. Next in order of convenience are university and high school students.

With regular and proper testing and supervision as outlined, and with the required co-operation, rarely has any tuberculous disease developed without sufficient warning. Where such extra rest as advised was taken, we cannot say that any disease has developed.

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The sustained co-operation of the Principal of our School of Nurses, first Miss Beatrice Ellis, and latterly Miss Gladys Sharpe, and the continuous support of our General Superintendent of the Hospital, Mr. A. J. Swanson, have been, of course, most essential, and keenly appreciated by the entire group responsible for our symposium.

We thank the following for constructive criticism and help in phraseology and arrangement of this paper: Doctors Harvey Agnew, R. D. Defries, D. T. Fraser, Wm. Goldie, W. L. Holman, Wm. Magner, P. A. T. Sneath, G. S. Young, Major George Shanks, all of Toronto, Prof. E. K. Brown of the University of Chicago, and the late Dr. H. C. Cruikshank.

Fourteen of the twenty-two authors of this paper have at one time or another been connected with the Department of Veterans' Affairs. All have much appreciated the facilities courteously afforded by the D.V.A. With these it has been possible to carry on twenty years of clinical research. This in turn has brought the practical application of the tests to a high degree of accuracy, as has been delineated in the text.

## RESUMEN DE LOS HALLAZGOS COINCIDENTES NO PERTINENTES DIRECTAMENTE AL TEMA PRINCIPAL

*(enumerados en el mismo orden que en el texto)*

1) Si se juzga que lesiones tuberculosas mínimas "silenciosas" o asintomáticas, descubiertas mediante exámenes radiográficos sistemáticos o colectivos, están posiblemente "estacionadas" o "aparentemente curadas," y si van acompañadas de reacciones normales del suero, se le permite al paciente que continúe en su trabajo mientras se llevan a cabo estudios serológicos adicionales. Si la gráfica de estas reacciones se torna desfavorable, se declara al individuo inhabilitado para trabajar y se prescribe un período de descanso; si la gráfica continúa favorable, no se le interrumpe el trabajo.

Se presenta el ejemplo de una joven que solicitaba ingreso a la Escuela de Enfermeras, a quien, en el examen radiográfico sistemático, se le descubrieron lesiones tuberculosas mínimas del parénquima de ambos vértices. Las reacciones normales del suero sanguíneo indicaron que no existía actividad potencial, y fue admitida a la escuela. Como quiera que durante todo su curso de instrucción las gráficas serológicas continuaron favorables, se le permitió que completara el curso de tres años, y la radiografía permaneció "in statu quo".

2) El período de incubación más corto observado en un caso de derrame pleural, que fue de tipo primoinfección, fue de cuatro meses. En Marzo de 1943 una niña de veinte años de edad resultaba negativa a 10 mg. de tuberculina; en Julio de 1943 existía un derrame pleural. (Sobrevino invasión de las meninges y falleció en Enero de 1944).

3) La exposición íntima más corta que, aparentemente, resultó en un caso de derrame tuberculoso de tipo primoinfección fue de seis horas. Una niña de veinte y dos años de edad era negativa a 10 mg. de tuberculina en Enero, la exposición ocurrió en el mismo mes y el derrame pleural apareció en el mes de Junio siguiente.

4) En la prueba con tuberculina, la dosis de 10 mg. es de valor bien definido pero de aplicación limitada.

5) Se define el término "Contacto con Tuberculosos," el que se clasifica también de acuerdo con el número de horas de exposición íntima.

6) La exposición íntima más corta de la serie, que resultó en un caso de tuberculosis (pulmonar) de tipo reinfección después de dos años y medio, fue de setenta horas.

7) El período de incubación más corto en un caso de tuberculosis pulmonar de tipo reinfección, fue de cuatro meses. La exposición íntima fue de mil horas.

8) Una dosis letal de bacilos tuberculosos, es decir, necesariamente fatal por sí misma (en el tipo reinfección), es rara en colectividades civilizadas e higiénicas.

9) Mientras mayor es la exposición íntima y más grande la dosis de bacilos tuberculosos recibidos, más corto es el período de incubación.

10) Se opina que, después de haber tenido lugar la infección, el mayor factor en el desarrollo de la enfermedad es la fatiga fisiológica. (Sólo le va en zaga a una posible dosis masiva).

11) Se duda de la supuesta disparidad en la resistencia innata a la tuberculosis entre las razas cobriza, negra, amarilla y blanca; probablemente los factores higiénicos son más importantes que la raza, puesto que ellos ejercen influencia, en primer lugar, sobre la dosis de infección, sea mínima, espesa o masiva, y, en segundo lugar, sobre la resistencia del individuo.

12) Se calcula que el período medio de incubación en el tipo reinfección es de cuatro a seis años.

#### RESUMEN

1) Cada 4 meses se prueba con tuberculina a los contactos con tuberculosos y a los estudiantes de enfermería. Cuando resultan positivos se les comienzan a hacer pruebas serológicas cada 4 meses.

2) Se considera que existen signos de peligro de afección tuberculosa cercana cuando sucesivas reacciones Inhibitorias o de Fijación producen ciertas gráficas serológicas positivas o significativas. Una gráfica que revela variación presagia un peligro más inminente que si es simplemente positiva. Se explica que es comprensible esto cuando se trata de reacciones de inmunología. Un marcado incremento reciente en la sensibilidad a la tuberculina aumenta lo precario de la situación.

3) Cuando se notan Signos de Peligro en las gráficas de enfermeras con horas normales de trabajo, les ordenamos que duerman durante sus horas libres del día y les suspendemos cuatro de los seis permisos mensuales de regresar tarde en la noche. Por lo general, esto hace desaparecer el peligro, y la enfermedad tuberculosa no se desarrolla. Empero, si después de varios meses de este reposo obligatorio no desaparece todavía el peligro, les cambiamos la receta a uno, dos o tres meses de cama en su casa. En cuanto a los contactos que trabajan las 7 u 8 horas diarias corrientes, suele ser suficiente adelantarles la hora ordinaria de apagar las luces de 12 p. m. a 11, o de 11 a 10; también puede añadirse el descanso en cama, un fin de semana sí y otro no. La omisión de este reposo resulta, tarde o temprano, en el desarrollo de tuberculosis en la mayor parte de estos sujetos.

4) Se exponen tres ejemplos de gráficas salvas: no hubo señales

de peligro, no se guardó descanso adicional y no se desarrolló la tuberculosis. Se presentan diez ejemplos de gráficas con presagios de peligro; cuando se guardó descanso adicional, las señales de peligro disminuyeron y no se desarrolló la enfermedad. Luego se muestran doce gráficas con avisos de peligro en las que no se guardó el descanso prescrito y si se desarrolló la tuberculosis.

5) Los dos factores principales en el buen éxito de este método son: primero, la exactitud en la interpretación de las pruebas; y segundo, la firmeza en prescribir el reposo por razones puramente hipotéticas y en ausencia de síntomas o de alguna irregularidad manifiesta.

#### CONCLUSIONES

Con un gasto relativamente pequeño, con la ayuda de un grupo de laboratorio clínico interesado en la medicina preventiva, y con plena cooperación, puede no haber tuberculosis en una colectividad. Debe ser posible dividir cualquiera colectividad en grupos apropiados, en cuanto a tiempo y lugar, para la conveniencia de las pruebas tuberculinicas y serológicas, de la instrucción y el control. Los grupos más fáciles de vigilar así son los de estudiantes de enfermería y los contactos con tuberculosos en clínicas del pecho. En orden de conveniencia les siguen los estudiantes universitarios y los de escuelas superiores.

Cuando se han llevado a cabo regularmente las pruebas y la supervisión, en la forma bosquejada, y cuando se ha obtenido la requerida cooperación, es muy raro que se haya producido afección tuberculosa sin suficiente advertencia. Cuando se ha guardado el descanso adicional prescrito, no podemos decir que se haya desarrollado ninguna enfermedad.

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# Thoracoscopy as a Method of Exploration in Penetrating Injuries of the Thorax (Preliminary Report)

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The examination of the thoracic cavity by endoscopy, always requiring a previous pneumothorax, was first performed on human beings by Jacobaeus, of Stockholm, in 1903. It had previously been performed by Kelling of Dresden, in 1901, on animals.

Jacobaeus commented upon the importance of this method in the study of pleural adhesions in patients with artificial pneumothorax and also drew attention to the possibility of severing these adhesions by means of the galvanocautery. This method also designated as Jacobaeus' Operation, is nowadays very well known and widely used.

Later the indications for thoracoscopy were broadened, but only a few years ago did it enter the general semiologic management of thoracic affections. Thoracoscopy renders possible the topographic diagnosis of tumors and their connections with the organs of the thorax, as well as the detection of adenopathies, subpleural blebs, miliary pleuritis and nodular pleuritis, anthracosis, fistulas, abnormalities of the organs and intrathoracic veins, etc. As it allows the direct exploration of the internal surface of the thoracic wall and of the organs and veins therein, it is strange that this new semiologic technique has not yet been used, as we have heard of no work dealing with this technique as a means of inspecting pleuro-pulmonary injuries in which a pneumothorax or hemopneumothorax developed, no matter how small, but sufficient to allow the introduction of the thoracoscope. By this simple method we are able to verify visually, whether the wound bleeds into the thorax, or whether there is a pulmonary lesion, with or without bleeding, as well as lesion of any intrathoracic vein, such as the internal mammary vein, subclavian, azygos, thoracic duct, etc. Finally, the detection of any serious lesion of vein or organ which calls for a wide emergency thoracotomy, in order to stop the hemorrhage. Even when a wide thoracotomy is necessary, thoracoscopy will indicate the localization, shape and extent of the incision, in order to allow a better approach to the lesions observed by endoscopy. In the absence of hemorrhage, or when it is discovered that

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the bleeding vein has already been obliterated, this method enables us to avoid thoracotomy, an operation which is much more serious than a thoracoscopy which only requires a simple small pleurotomy. It further enables us to find out whether or not there exists injury to the diaphragm with the possibility of damage to an abdominal organ or vein, requiring laparotomy; and also to discover whether on the left side there exists a wound in the pericardium, with probability of a lesion of the myocardium requiring, in either case, a quick intervention for its suture.

When blood is found in the pleural cavity, we draw it out by means of the trocar used for thoracoscopy, and we gather it in sterile glasses, and after filtration through gauze, we use it again for reinfusion, as it is very well known that blood extravasating into the serous spaces does not coagulate. For the reinfusion we use a Joubé syringe, generally used for blood transfusions. In a previous work in collaboration with Aresky Amorim, we have already stated our point of view as to the danger of contamination of the blood extravasating into the thorax, in cases of penetrating injuries. As there exists a communication with the exterior, whether through the parietal or pulmonary injuries, whether through visceral trauma which causes hemorrhage and the entry of air into this cavity, it is natural to fear contamination of the hemothorax. Yet, as reinfusions are generally performed a few hours after the occurrence of accidents, there is no time for the multiplication of microorganisms and their diffusion in the blood to be reinfused. And the few bacteria which might be carried into the circulatory system would be destroyed in the blood itself or rendered inactive by the reticuloso-endothelial system. This fact is supported by experience, according to the observation below, where reinfusion was performed 27 hours after a chest injury.

#### CASE REPORTS

**Case 1:** A.S., Male, Negro, single, laborer, Brazilian, aged 23. Entered the Emergency Hospital at 10 P. M. on November 16, 1944. Penetrating injury to the right hemithorax with consecutive hemopneumothorax. A 4 cm. wound had already been sutured at the level of the fifth right intercostal space, midclavicular line. He stated he was attacked with a knife at 8 P. M. the night before. Pulse, 92; auxillary temperature, 36.9° C; blood pressure, 125 over 75.

At 11:10 P. M. a right thoracoscopy was performed. Introduction of the trocar in the third intercostal space, at the level of the anterior auxillary line. Aspiration through a rubber catheter, of 370 cc. of blood which, after filtering through gauze, were used for reinfusion. The examination of the thoracic cavity showed a small wound in the front part of the middle lobe, with closed margins and small clot all around. The internal surface of the parietal wound was not bleeding. Small quantities of sanguineous clots at the bottom of the pleural cavity. Diffuse antracosis on the whole pulmonary surface. Withdrawal of the

trocar during forced inspiration, and suture of the wound of the thoracic wall in two plans, without drainage. Normal post-operative course. Twenty days later patient left the hospital entirely recovered and with the lung completely re-expanded.

When thoracoscopy, after the removal of the blood in hemothorax, shows the existence of pulmonary lesion which no longer bleeds or is bleeding very little, and does not require thoracotomy to be sutured, as in the above observation and in the following one as well, the trocar is removed from the thorax during forced inspiration. Acting in such a way we leave a pneumothorax which, keeping the lung collapsed, prevents the continuation of the hemorrhage and facilitates cicatrization of the pulmonary wound.

Case 2: W.P., male, white, Brazilian, single, shop employe, 24 years old. Entered the Emergency Hospital at 7:50 P. M., February 20, 1945. Penetrating wound of the right hemithorax, with consequent hemothorax by bullet of fire-arm. Entrance opening at the level of the mammary region and exit at the level of the seventh intercostal space, slightly below the angle of the scapula. Patient was in Schock. Pulse rate, 136; blood pressure, 90 over 40. Right thoracoscopy at 2 A. M., February 21, 1945. Introduction of the trocar in the third intercostal space, at the level of the anterior axillary line. Spontaneous evacuation of blood and, afterwards, aspiration through a rubber catheter of 500 cc. of liquid blood and small clots. Filtration of the blood through gauze and reinfusion of 300 cc. thereof. Washing out of the pleural cavity with lukewarm physiologic saline in order to remove the remaining clots. Examination of the pleural cavity, with direct and indirect vision, showed the pulmonary surface covered with small sanguineous clots. The wounds existing in the front and back walls of the thorax were bloodless. A small wound was observed in the front part of the upper lobe, with closed margins, which was not bleeding. It was not possible to locate the exit opening in the lung. On completing the surgical operation the pulse was 100 per minute and the blood pressure 120 over 75. Patient left the hospital recovered on March 3, 1945, eleven days after the accident, with the lung completely re-expanded.

If after removal of the hemothorax, the endoscopic examination of the pleural cavity shows that the blood comes from the intercostal vein, liable to be connected by simple débridement of the wound, and further, showing no pulmonary lesion, we withdraw the trocar during maximum expiration, in order to provoke quick re-expansion of the lung, as it was done in the next case below:

Case 3: A.F.S., male, white, Portuguese, married, blacksmith, 48 years old. Entered the Emergency Hospital at 11:10 P. M. on the 2nd of May 1943. Penetrating wound of the right hemithorax, with consequent hemothorax. He told us he had been wounded with a knife, half an hour before. A wound, 3 cm. wide was found, located 2 cm. from the border of the sternum, at the level of the third intercostal space. Radial pulse more or less tense, 112 per minute. Pale, sweating profusely, blood pressure 100 over 60. Right thoracoscopy was performed two hours after

the injury. Introduction of the trocar at the level of the axilla. Spontaneous evacuation of blood and followed by aspiration of 650 cc. of blood, which, after filtration through gauze, were at once reinfused. The thoracoscopic examination showed a wound of the parietal pleura, of about 1.5 cm. long, perpendicular to the border of the sternum and about  $\frac{1}{2}$  cm. from the internal mammary veins, through which bleeding was noted irregularly. No wound found on the pulmonary surface. Pronounced anthracosis of the upper lobe. The lung was covered, in a few places, with small blood clots. Costophrenic sinus free. Removal of trocar during maximum expiration. Subsequent débridement and suture of the parietal wound, when it was found that the hemorrhage was originating from the intercostal vein which was connected. Closing of the wound in two planes with catgut, without drainage. Tight dressing. Upon completion of the operation the pulse was 90 per minute and blood pressure was 115 over 70. Postoperative course was uneventful. Patient left hospital completely recovered nine days later, with the lung completely re-expanded.

The considerably expansibility of the lung in certain cases, and more especially in young patients and in emphysematous cases, as well as the presence of adhesions and partial symphysis not allowing the formation of a large pneumothorax, sometimes render difficult a thorough examination of the pleural cavity. Same occurs with patients with hemopneumothorax, in which, after the removal of the blood a few clots are left in the pleural cavity, which cover the optic system at each moment and thereby impair the visibility. In the latter case it is advisable to wash the pleural cavity with lukewarm physiologic saline, in order to remove the clots. This is what occurred in the observation below:

Case 4: A.S., male, white, Brazilian, single, shop employed, aged 18. Entered the Emergency Hospital at 9:10 P.M., November 18, 1943 with a penetrating wound of the left hemithorax and with a consequent hemothorax. Tried to commit suicide a few minutes before. Pale, with discolored mucosa. Sweating intensely. Vomiting food with traces of blood. Filiform pulse, 144 per minute; blood pressure, 100 over 65, Tachypnea, 34 per minute. Left thoracoscopy performed about one hour after the incident. Introduction of the trocar in the fourth intercostal space, at the level of the midaxillary line. Spontaneous flow of blood and afterward, aspiration through a rubber catheter of 720 cc. of blood, used for reinfusion. Thereupon thoracoscopy was performed, but it was handicapped not only owing to the existence of a small pneumothorax, but also because of the presence of a great quantity of blood clots. The pleural cavity was washed out with lukewarm physiologic saline, in order to remove the clots. Re-examination of the pleural cavity again was negative, even with the use of indirect vision. Removal of trocar with maximum inspiration. Normal postoperative course. Patient left hospital completely recovered 10 days after suicide attempt. Lung completely re-expanded.

Case 5: V.S., male, Negro, Brazilian, single, laborer, aged 24. Entered the Emergency Hospital at 5:05 P.M. on September 3, 1944. Penetrating wound in the left hemithorax, with consequent hemopneumothorax. He

told us he had been attacked with a dagger half an hour before. Examination of the patient showed a wound about 2 cm. long at the sixth left intercostal space, three fingers from the border of the sternum, with subcutaneous emphysema around it. Pale, sweating intensely and very thirsty. Rapid, soft pulse, 120 per minute; blood pressure, 80 over 50. Axillary temperature, 36° C. Left thoracoscopy one hour after patient's arrival at hospital. Introduction of the trocar in the sixth intercostal space in the midaxillary line. Spontaneous evacuation of blood and afterwards, aspiration through a rubber catheter of 1000 cc. of blood, of which 950 cc. were reinfused after filtration through gauze. Washing out pleural cavity with lukewarm physiologic saline. Lung very expanded and interfered with the examination. Patient was coughing and breathing deeply every minute, sometimes expelling the cannula from the thorax. Removal of trocar during maximum expiration. Débridement and suture of the parietal wound, with connection of small little arteries which were bleeding into the thorax, owing to negative intrapleural pressure. Normal postoperative course. Left hospital recovered, with lung entirely re-expanded, 20 days later.

#### SUMMARY

As we have shown above, and according to the observations stated, thoracoscopy renders us important services as an exploratory method in penetrating wounds of the thorax, accompanied by pneumothorax or hemopneumothorax. We have been using this method since May 1943, the date of our first observation, which was followed by four more. Our five patients left the hospital recovered, without undue consequences, with lungs re-expanded, after 20, 11, 9, 10 and 20 days, respectively. Unfortunately, we have only been able to observe a few of the many aspects of penetrating wounds of the thorax. But I feel certain that thoracoscopy will be very useful for the diagnosis of all varieties of such wounds.

#### RESUMO

O A. propõe, no presente trabalho, o exame da cavidade torácica, por via endoscópica, como método de rotina, nas feridas penetrantes do tórax complicadas de pneumo ou hemopneumotórax. Assinala como vantagens dessa nova técnica a facilidade com que se pode verificar, *de visu*, se o ferimento sangra para dentro do tórax. A existência de lesão pulmonar, com sangramento ou não. Lesão de qualquer vaso intratorácico, como a mamária interna, subclávia, ázigos, canal torácico, etc. Enfim, a constatação de qualquer lesão grave, de vaso ou de órgão, que justifique uma toracotomia larga de urgência, afim de se coibir hemorragia. E, ainda, verificada a necessidade de uma toracotomia larga, tem a vantagem de orientar a situação, fórmula e extensão que se deverá dar à incisão, afim de permitir uma melhor abordagem das lesões observadas pela endoscopia. Ou, então, constatada a ausência de hemorragia, ou verificado já se encontrar obliterado o vaso que sangrava, prescindir de

uma toracotomia exploradora, operacão indubitavelmente muito mais grave do que uma toracoscopia, que requer unicamente uma simples pleurotomia mínima. Permite ainda, verificar se existe ou não lesões diafragmáticas, bem como pericárdicas, se á esquerda, autorizando laparotomia ou via de acesso ao coração, conforme o caso. Havendo hemotórax, propõe o A. o aproveitamento do sangue para reinfusão, justificando o seu ponto de vista. O trabalho é documentado com cinco observacões. A toracoscopia foi realizada em todos doentes, fornecendo interessantes e preciosos dados diagnósticos, que orientaram a terapêutica a seguir em cada caso. A reinfusão do hemotórax foi sempre praticada, nunca ocorrendo acidentes nem complicacões.

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## Tuberculosis Among Sanatorium Personnel

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There are few instances of mass studies as rewarding as that of the incidence of tuberculosis among people working in sanatoria and hospitals. The ideas about contagiousness, effectiveness of exposure and protective measures are subject to the hardest trial within a field particularly well controlled. After a few years of experience according to a definite plan, one is able to gather specific facts, and if the experience is planned in such a way as to bring proof for an hypothesis, the test in the sanatorium is a true scientific experiment. The personnel for a sanatorium may be chosen according to the requirements that the student considers adequate for control. Age, previous health conditions, Roentgen inspection, education on the protective measures, etc., may be regulated before the exposure starts. Furthermore, the exposure to tuberculous infection is regularly effected for the same number of hours under the same conditions every day and the protective measures are part of the routine in the institution.

This subject has been studied in many institutions in various parts of the world and the results have been reported so they are widely known. If it were not for the astounding results of our survey, the insistence upon these matters would be trivial.

It is a commonly known fact that tuberculosis among nurses, doctors and other members of sanatorium personnel is much less frequent than might be expected from their exposure to contagious cases. This frequency, however, is higher than the expected morbidity among the population in groups of the same age living in the same region. Exposure to tuberculous infection is admitted as a real risk for the sanatorium's employees and the measures against infection have been more and more strict.

Gordon and Cashman, studying 737 employees and former employees of a tuberculosis hospital, including 66 resident physicians, 48 visiting doctors and 566 nurses, found only thirteen cases in which the diagnosis of tuberculosis was made. They concluded that the incidence is under 2 per cent. Shipman and Davis made a survey among the students of nursing at the University of California and found that from 6 to 7 per cent became ill from tuberculosis. Heimbeck, at the Ulleval Hospital of Oslo, observed

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tuberculin reactions among entering students of nursing and each year thereafter until the end of the training period. On entering the school of nursing the incidence of tuberculin reactors was 50 per cent; on graduation it was 100 per cent. The incidence of demonstrable lesions which developed is as follows:

|                      | <i>Nonreactors</i> | <i>Acquired<br/>Tuberculosis</i> | <i>Reactors</i> | <i>Acquired<br/>Tuberculosis</i> |
|----------------------|--------------------|----------------------------------|-----------------|----------------------------------|
| Probationers in 1924 | 51                 | 17                               | 58              | 1                                |
| Probationers in 1925 | 72                 | 21                               | 42              | 1                                |
| Probationers in 1926 | 62                 | 15                               | 52              | 1                                |

Until June 1931 there were eighty-one nurses with signs of tuberculosis, seventy-one of whom were nonreactors on entrance to the school of nursing.

The work of Geer at the Ancker Hospital in Saint Paul, Minnesota, revealed that among 181 nurses entering training from September 1930 to June 1932, only three (1.6 per cent) became sick with tuberculosis. These were nonreactors before the hospital exposure. This low rate is considered the result of extreme measures for the protection of students. During the years prior to this survey the rate was 4.5 per cent, or triple the expected morbidity among women of the same age in that city. Among 112 nurses who entered training from September 1928 to September 1930, six (5.5 per cent) acquired tuberculosis, five of whom were nonreactors before their hospital exposure.

Myers stated that more than 11 per cent of the students entering a school as non-reactors in 1929 had demonstrable lesions in 1934. At the Fitzsimons Hospital in Denver, Pollock and Forsee observed 227 physicians, nineteen dentists and 518 nurses over a ten year period. All were tuberculin reactors and had evidence of old primary infection. Among the physicians, four (1.7 per cent), the dentists, one, and the nurses, eight (1.3 per cent) developed clinical tuberculosis.

Ornstein and Ulmar, from 1931 to 1936, made a survey among 1000 nurses at the Sea View Hospital. Thirty-one (3 per cent) developed demonstrable lesions, but only twenty-one (2 per cent) during their stay at the hospital. Morbidity among those in other occupations outside the hospital was from 0.09 per cent to 1.1 per cent. These authors conclude that the average morbidity among nurses in a tuberculosis hospital is about 2 per cent and is higher than that expected among people of the same age.

Israel and Hetherington reported on the findings among 643 white nurses at the General Hospital of Philadelphia. Demonstrable lesions appeared in 12.3, 12.6 and 6.2 per cent among those who entered as nonreactors, those who reacted to 0.005 milligrams and

those who reacted to 0.00002 milligrams of PPD, respectively.

Hastings and Behn reported 706 nurses, among whom 2.2 per cent presented lesions in three years. The nonreactors on admission to the schools showed lesions three times more frequently than the reactors. Hahn and Munscheim stated that among 2952 student nurses in a general hospital, forty-nine (1.7 per cent) present lesions.

*The Method at the Tuberculosis Sanatorium of Huipulco, Mexico*

In an attempt to control tuberculosis among the personnel of our sanatorium, we adopted the following procedures:

1. All persons accepted for work at the sanatorium must be over twenty years of age.
2. Employees must be tuberculin reactors.
3. A roentgenogram must be available on employment and annually thereafter.
4. Complete physical examination was kept on a special form in the record.
5. Whenever any illness occurred among the personnel, a new physical examination must be made and a new chest film taken, regardless of the apparent relationship of the condition with tuberculosis.

The personnel was classified according to the exposure, into three groups:

1. Those highly exposed (doctors, nurses, maids, orderlies, etc.).
2. Those who incidentally came in contact with patients (pharmacists, electricians, masons, painters, etc.).
3. Those never exposed, such as cooks, some clerks, etc.

The survey comprised among the highly exposed 357 employees, as follows:

|                               |     |
|-------------------------------|-----|
| Physicians                    | 30  |
| Dentists                      | 2   |
| Nurses                        | 93  |
| Maids                         | 101 |
| Laundry and disinfection work | 30  |
| Orderlies                     | 44  |
| Laboratory technicians        | 2   |
| Barber                        | 1   |
| Gardeners                     | 13  |
| Clerks                        | 5   |
| Repair shop                   | 11  |
| Watchmen                      | 25  |

There were 135 unexposed or exposed only incidentally.

About 80 per cent of the personnel showed Roentgen ray evidence of residual primary infection of more or less extensive local fibrosis from old reinfections. The remainder of the films were

normal. There was no case of active tuberculosis among the workers before they started their contact.

There are now 225 members of personnel for a 350 bed sanatorium. During the eight years under consideration 492 people worked at the Sanatorium in different positions for variable periods of time, from several weeks to eight years. Among the 357 highly exposed, only two maids, one gardener and one orderly developed the reinfection type of tuberculosis. This is 1.1 per cent. None of the other two groups developed demonstrable lesions.

The following points are worthy of special mention: All persons working at the Sanatorium were tuberculin reactors except two, for reasons beyond our control. One of them remains a nonreactor; the other, an orderly, developed an apical infiltration with hemoptysis. Acid-fast bacilli were recovered from the stomach washings but not from the sputum. The two maids who developed lesions never had tubercle bacilli in the sputum. They recovered in a few months and resumed their work. The gardener had a round infiltrate twenty days after starting his work; no film was available before, so this remains a doubtful case.

#### SUMMARY

Only four infiltrates thought to be tuberculous, one of which was open tuberculosis, were discovered among 357 highly exposed people during eight years.

The results of our experience confirm our belief that the measures adopted before the opening of the Sanatorium were justified. Therefore we believe that the main factors for protection against reinfections among personnel are:

- 1) Evidence of an old lesion, the older the better, as demonstrable by the residual roentgen appearance.
- 2) The lesion must be apparently extinguished but the tuberculin test ought to remain positive.
- 3) The personnel must be selected among people over twenty years old. This measure makes, at least in Mexico, more possible an old infection to be completely inactive.
- 4) All exposed people must have well balanced diet, limited number of working hours, and should be instructed to protect themselves against infection.
- 5) The sanatorium must be built so as to allow many hours of exposure to the sun so as to afford the effect of the ultraviolet rays on contaminated surfaces.

If these rules are followed, it is possible to obtain results such as ours, which seem rather paradoxical, as the workers at the tuberculosis sanatorium become reinfected less frequently than the population in the City of Mexico, where the expected mor-

bidity is 1.3 per hundred, while it is zero in our nurses group and under 1 in the highly exposed people. The educational standards, habits, hygienic way of living and diet are very much lower than the American level among our personnel, excepting physicians.

#### RESUMEN

Pocas oportunidades se presentan al investigador de la tuberculosis para definir sus ideas sobre la contagiosidad, la efectividad de las medidas protectoras y el riesgo de la exposición, como la observación de lo que ocurre con los que trabajan con una exposición a la infección tuberculosa que es atributo profesional de su vida.

La observación de la influencia de la exposición se transforma en una fructífera experiencia cuando se regulan las condiciones de los sujetos antes de someterlos al peligro de la infección y cuando se ponen en juego las medidas protectoras, cuya aplicación constituye una verdadera experiencia clínica.

La experiencia del Sanatorio de la Asistencia Pública de México cuyos empleados han sido controlados desde el punto de vista de su salud general y de modo especial con respecto a la tuberculosis, es relatada después de un lapso de ocho años.

Es un hecho reconocido generalmente que la tuberculosis entre el personal de los sanatorios es mucho menos frecuente de lo que era de esperarse dada la constante exposición al contagio de los trabajadores. Sin embargo la frecuencia de la tuberculosis activa entre los que trabajan en los hospitales de tuberculosos es habitualmente más alta que la de la población de la región y todos los autores están de acuerdo en que es necesario tomar medidas para evitar la aspiración de gérmenes por parte de los expuestos al contagio.

Se relatan en esta comunicación los trabajos de varios autores sobre el mismo asunto, tales como los de Gordon y Cashman, Shipman y Davis, Everett Geer, Myers, Pollock y Forsee, Ornstein y Ulmar, Israel y Hetherington y Hasting y Behn.

En el Sanatorio de la Asistencia Pública de México, desde su apertura en 1936 se siguió un método de observación y de investigación sistemático que comprendió a todos los trabajadores, empleados y médicos que durante más de ocho años han estado en contacto con tuberculosos en grados variables.

Las medidas protectoras que se tomaron fueron en resumen las siguientes: (a) Todos los expuestos al contagio en el Sanatorio deben ser mayores de 20 años de edad.

(b) Todos los empleados deben tener una reacción de Pirquet o de Mantoux positiva.

(c) Deben ser radiológicamente sanos aunque tengan aspectos radiológicos de secuelas de tuberculosis antigua. (Primoinfección, pleuritis, fibrosis).

(d) Se sujetan a examen general a fin de eliminar a los que tienen enfermedades no tuberculosas que los incapaciten.

(e) Se hacen radiografías iniciales y con intervalo de un año o menos a todos los empleados y siempre que hay algún trastorno de su salud, aunque no aparente ser de naturaleza tuberculosa, se les hace una radiografía de tórax.

Se clasificó el personal por su grado de exposición en tres grupos: El primero, de altamente expuestos, incluye médicos, enfermeras, sirvientes de todas clases. El segundo grupo incluye los que tienen exposición accidental pero poco frecuente. El tercer grupo corresponde a los que no tienen exposición sino de manera rara y no profesional necesariamente.

La investigación incluyó durante ocho años a 337 empleados muy expuestos, 135 poco expuestos y raramente expuestos. Ochenta por ciento de los empleados mostraba residuos de infección tuberculosa extinguida, ya sea de primo o de reinfección.

En total se estudiaron 492 personas expuestas en grados diversos.

|     |                            |      |
|-----|----------------------------|------|
| 30  | Médicos                    | 0    |
| 2   | Dentistas                  | 0    |
| 93  | Enfermeras                 | 0    |
| 101 | Sirvientes (afanadoras)    | 2 2% |
| 41  | Trabajadores de lavandería | 0    |
| 13  | Jardineros                 | 1    |
| 44  | Mozos                      | 1 2% |
| 34  | Diversos                   | 0    |

En todo este grupo de muy expuestos hubo 4 casos entre 357 o sea un porcentaje de 1.11. En todo el personal la proporción de reinfecciones es de 0.89 por ciento.

Es de notarse que el único caso que por circunstancias fuera de control trabajó teniendo una reacción de Pirquet negativa está entre los cuatro casos infectados.

El término medio de las personas que están en contacto con tuberculosos y que se infectan, lo hacen en la proporción de 2 por ciento según la mayor parte de los autores.

Si en el Sanatorio se obtienen cifras más bajas de tuberculosis entre los empleados, se atribuye esto a la eficacia de las medidas tomadas para proteger a los empleados, a las que hay que agregar la situación del Sanatorio, a gran altitud, con gran aereación y asoleamiento que hace la desinfección de los pisos por la radiación solar, un fenómeno constante.

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## The Epidemiology of Tuberculosis in Brazil and Vaccination with B.C.G.

MARCIO M. BUENO\*

*Rio de Janeiro, Brazil*

Brazil, country of vast extent, with an area of more than 3,250,000 square miles, and a comparatively small population, about 45,000,000 inhabitants, is to a great degree, as regards to tuberculosis, in the full stage of massive tuberculization. The rate of mortality for tuberculosis is 250 for 100,000 inhabitants. The greater part of the Brazilian population live along the coast, more densely crowded in the south. Also, there are cities and towns in the interior where tuberculosis is now beginning to penetrate. These are in the stage of "pre-tuberculization"—mortality and illness rates are low, but on the increase, the index of infection is still quite low. As an example: Theresina and Cuyaba, capitals of the states of Piauhy and Matto Grosso (70 per 100,000 tuberculosis mortality).

The leading cities, situated on the coast, and those cities with good communications, are in the epidemic stage (Recife, capital of Pernambuco has a tuberculosis mortality rate of 400 per 100,000), except Sao Paulo, which is already at the stage of "detuberculization," changing from the epidemic to the endemic phase which is easy to explain because the population of Sao Paulo consists, in the great majority, of descendants of Italians, people who have already reached the endemic stage after passing through the massive stage.

The fight against tuberculosis in Brazil, as we can see, calls for a great deal of equipment, much more than in countries that have passed through the epidemic stage of tuberculosis and have reduced their death rate to a minimum. This residual or basic rate through the mass x-ray survey of the chest made possible by the photo-fluorography of the Brazilian physician Manuel de Abreu, can be eliminated. The non-apparent cases can be detected. Early diagnosis and early treatment is the goal in countries which are in the endemic stage. Among us the situation is different and the equipment available for the battle against tuberculosis is unfortunately very inadequate. To give only one example: Minas Geraes, fifth state in area, and second in population, with 8,000,000 inhabitants (250 per 100,000 tuberculosis mortality), a rich and productive state, has only two dispensaries, one in the capital and

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the other in Juiz de Fora, both maintained by the State Government. There are dispensaries without Abreu apparatus (35 mm.), the static type of dispensary, who hope the sick man will come to seek them; without visiting-nurses—at least not in numbers sufficient—to do adequate work. With respect to beds, Minas Geraes has only about 200 for the tuberculous indigent, supported by special associations, and 450 more for paying patients in special sanatoria. It should be noted that in Minas Geraes, because of its climate, the capital and the city of Palmyra are much sought after by large numbers of tuberculous patients from other parts of the country. The State of Sao Paulo and the Federal District possess the best anti-tuberculosis equipment, but even they have not enough. We do not have sufficient number of beds where the contagious cases may be isolated and treated. On the other hand, we have a high rate of cases of serious primary progressive infections. The average of non-allergic people is high in the provincial regions. Whoever studies the mortality rate for tuberculosis in Brazil, must observe the following: the mortality curve for tuberculosis is high in the first two years of life, then falls, and rises once more in adolescence, falling again after the age of 25. They are the ages of close contact of the children and growing adolescents with patients. The necropsies done by Reginaldo Fernandes and his collaborators in the Pedro de Almeida Magalhaes and Miguel Pereira—Hospitals in Rio de Janeiro, show the existence of a great number of primary progressive tuberculosis in young adults.

The studies of Heimbeck and Scheel in Scandinavia, followed by similar ones in other European countries, demonstrate irrefutably the seriousness of primary tuberculosis in adults. The non-allergic get sick and die in far greater numbers than the ones with previously acquired allergy.

The battle against tuberculosis in South America, as Sayago has already stated, is a battle against primary infection. But if people can be rendered "allergic" through a mild and controlled primary infection they will resist later infections.

This is possible through vaccination with B.C.G. Undoubtedly one of the most complete experiments about B.C.G. in the world were carried out in Brazil under the direction of Arlindo de Assis. Experiments with B.C.G. on human beings were begun by Weill-Halle in Paris in 1921 and by Assis in Brazil in 1927. From 1927 until December 1944, 164,152 persons were vaccinated in Rio de Janeiro, and 41,296 are under control. In all Brazil, we have over 340,000 who have been vaccinated. Today, no one disputes the innocuousness of B.C.G. and claims to the contrary are baseless.

Assis and Fialho inoculated heavy doses of heat-killed B.C.G. combined with paraffin oil in the testis of rabbits and they ob-

served a great deal of cellular proliferation, a high power of stimulation of the reticulo-endothelial system, without caseation which is characteristic of the lesions caused by virulent bacilli.

As to its efficacy, the most convincing proof is in the observation of vaccinated and non-vaccinated individuals living in the same environment. This study was made by Alvimar de Garvalho, observing 38 families, and showed that vaccinated individuals had a much lower tuberculosis morbidity and death rate than the non-vaccinated ones.

38 Families (48 children vaccinated.  
(58 children not vaccinated

|                         | Healthy | Sick<br>Tbc. | Morbidity |      | Mortality<br>Per cent |
|-------------------------|---------|--------------|-----------|------|-----------------------|
|                         |         |              | Per cent  | Tbc. |                       |
| Children vaccinated     | 38      | 10           | 20.8      | 1    | 2.1                   |
| Children not vaccinated | 32      | 21           | 39.6      | 7    | 13.2                  |

*Causes of death:*

Vaccinated—primary pulmonary progressive complex  
(first year of life).

Not Vaccinated—5 acute miliary tuberculosis,  
2 primary pulmonary progressive complex.

All the families had a source of contagion. This study was made from 1932 to 1937.

At the present time Assis is watching 1,426 families with tuberculosis, among these there are 2,050 vaccinated children and 2,598 non-vaccinated children. This study until now has the same conclusions as that of Carvalho. Another interesting observation in Rio de Janeiro was done by Aguiar and Rezende. In a survey in several districts of Rio de Janeiro where the proportion of children is 70 per cent vaccinated to 30 per cent of not vaccinated they found active tuberculosis in the proportion of one vaccinated child to five not vaccinated. The contrast is very conclusive. Assis has now vaccinated over fifty per cent of the new-born in Rio de Janeiro.

Our service is maintained in Rio by the Ataulfo de Paiva Foundation (Brazilian League Against Tuberculosis), a special institution receiving some aid from the state. The vaccine is prepared in special laboratories, with bacilli derived from the original culture with which Assis began his studies. This is rigorously checked by successive inoculations of animals. The Foundation has a competent corps of nurses who administer the vaccine at home or in the hospitals at no expense whatsoever to the patients. Those vaccinated are checked by the Foundation every year. They are submitted to clinical, radiologic, bacteriologic examinations and tuberculin tests. Assis prefers oral vaccinations, increasing the

initial dose of Calmette from 3 centigrams (1 ctgr. each time) to nine centigrams. In adults, Assis has administered up to 20 ctgrs. without unfavorable results, and to non-allergic children in the Preventorium of the Foundation, he has administered daily doses of 2 ctgrs. to a total of .96 to 1.32 gram and saw no disturbance whatsoever. Assis made an experiment on himself, injecting about 2 grams of B.C.G.; no untoward reactions followed. Assis prefers to administer B.C.G. in fresher cultures, with 12 to 14 days. Calmette recommended cultures of 25 days.

Assis considers that those who distrust oral vaccination employed small doses of old cultures. Other methods are more troublesome and make a very bad impression on those vaccinated and their relatives (subcutaneous, intradermic and multiple punctures). The question of the duration of allergy after the administration of B.C.G. given orally, is of no importance. Today the existence of latent allergy or infratuberculinity has been clearly demonstrated. Allergy is quite distinct from immunity (or refractory stage, as Assis prefers to call it). This has been shown by Willis and by Saye. Individuals who do not react to tuberculin, apparently non-allergic, have a considerable shortened period of pre-allergy when reinoculated. This was also demonstrated by Sayago and Degoy (Cordoba, Argentina), with re-vaccinations accelerated by B.C.G. Saenz and later Sayago studied the infratuberculin allergy by the vaccinations with B.C.G. of apparently non-allergic old men.

The vaccination of adults (voluntary in all Health Centers of Brazil), is always done after tuberculin tests and search for infra-tuberculin allergy, by Assis' own technique, with doses of heat-killed B.C.G. A reasonable percentage of infra-tuberculinity has been found. In the ones vaccinated with B.C.G. and apparently non-allergic, Assis found 76.2 per cent of infratuberculin allergy.

Seven states have their own laboratories for making the B.C.G.—the vaccine is sent by air to all the other states. All follow the procedure of Assis. The National Tuberculosis Division of the Public Health Department officially adopted the B.C.G.

There is no doubt that in the countries in the epidemic stage of tuberculosis, it will be impossible to secure in the near future, the construction of hospitals and sanatoria in sufficient numbers, at least, a minimum of one bed for each death from tuberculosis. The mass vaccination of non-allergic people with B.C.G. along the lines laid down by Assis is in Brazil one of the most efficient weapons in the battle against tuberculosis. In countries in the endemic stage, vaccination with B.C.G. is necessary for all non-allergic persons who must work or study in environments which are conducive to contagion. Medical students, student nurses, if non-allergics, should be systematically vaccinated with B.C.G.

## RESUMO

O autor passa rapidamente em revista a situação epidemiologica do Brasil no referente á tuberculose. Mostra as deficiencias do aparelhamento antituberculoso devido principalmente ás dificuldades financeiras. Cita o exemplo de Minas Geraes, sem duvida alguma um dos mais importantes estados da Federacão. Com dados epidemiologicas e anatomicos comprova a afirmativa de Sayago, de que a luta contra a tuberculose na America do Sul é a luta contra a primo-infeccão. Sumarisa o que se fez a propósito de B.C.G. no Brasil e realca os méritos de Arlindo de Assis. Finalisando, opina que nos paizes que se acham na faze epidemica da tuberculose, o B.C.G. deverá ser administrado a todos os anallergicos. Nos paizes onde a tuberculose está na faze endemica, deverão ser vacinados aqueles que terão oportunidade de viver em meio contaminado.

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## Experiences with B.C.G. in Latin America\*

FERNANDO D. GOMEZ, M.D.

*Montevideo, Uruguay*

The position of B.C.G. as a prophylaxis in the armamentarium against tuberculosis was one of the three official subjects discussed at the Sixth Pan American Congress on Tuberculosis at Havana, Cuba.

A committee comprised of the physicians who presented their experiences with B.C.G. reached the conclusion that the clinical and experimental possibilities of B.C.G. as well as its efficacy and innocuousness in immunization against tuberculosis have been demonstrated and confirmed, and made the following recommendations:

1. The use of the vaccine starting with the first day of life was advised either orally or parentally. Special emphasis has been placed on the necessity of preventing infection immediately following the administration of the vaccine.
2. In order to identify those children who have been vaccinated and to recognize immediate and later results of the vaccination, it has been advised that the method and technique of tattooing as used by Gomez and Etcheberry be followed.
3. To re-vaccinate periodically those children who remain tuberculin negative after a lapse of time.
4. It was recommended that laboratories be created in each country in order to standardize the preparation of the B.C.G. vaccine.
5. B.C.G. vaccine should be complemented by all the other prophylaxis and known means of proper care.

Tuberculosis is the most important medical, social and economic problem in Latin America and it requires a prompt solution.

Since 1927 much information has been gathered from over 500,000 clinical observations in the use of B.C.G. in Argentina, Brazil and Uruguay. This is the first time in the history of medicine that such favorable opinions about the efficacy and the innocuousness of B.C.G. have been stated by a group of outstanding chest specialists concerned with this important work. It is reported that to date these vaccinations are administered widely in most of the South American countries.

In Uruguay there are over 160,000 children vaccinated with B.C.G.

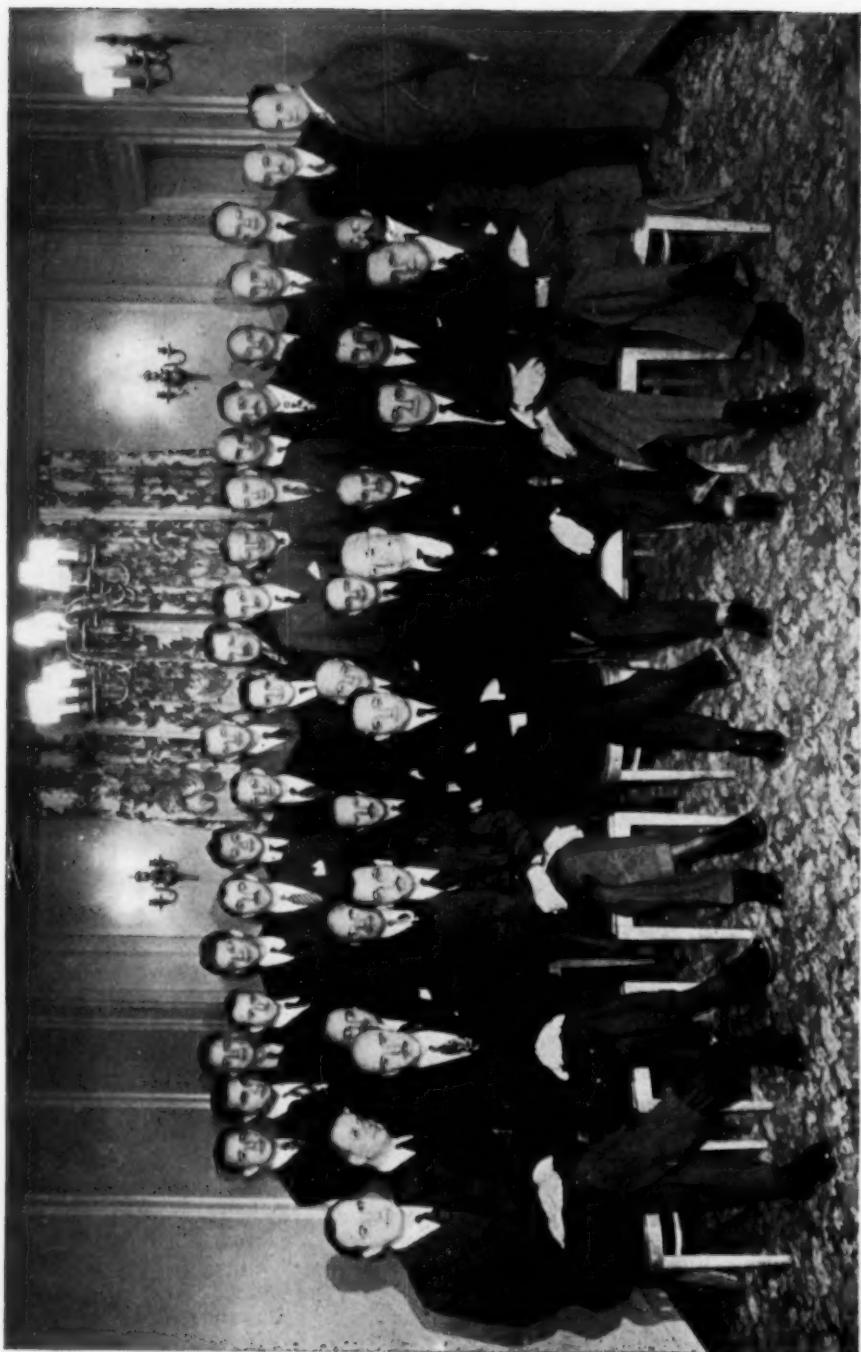
\*Notes from the Sixth Pan American Congress on Tuberculosis, Havana, Cuba, January 15-21, 1945.

and the vaccine is given systematically in the most important maternity hospital of the country, in which 30 per cent of the children of Montevideo are born (11 per cent of all the children born in the entire country). All of the newly born since 1940, totalling 17,000 children, have been vaccinated with B.C.G. and tattooed with indelible ink on the plantar aspect of the large toe of the left foot. This tattooing makes possible the identification of any vaccinated patient, living or upon necropsy.

Our analysis reveals that the mortality from tuberculosis among the vaccinated children is one-sixth that among un-vaccinated children who attend the same clinics and hospitals.

The experiences with B.C.G. in Uruguay warrant the statements made in this report and we concur with the conclusions arrived at by the other investigators as reported at the Sixth Pan American Congress on Tuberculosis at Havana, Cuba.

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INSTRUCTORS AND PHYSICIANS PARTICIPATING IN THE POSTGRADUATE COURSE IN DISEASES OF THE CHEST, MICHAEL REESE HOSPITAL, CHICAGO, ILLINOIS, APRIL 1-5, 1946

## Postgraduate Course in Diseases of the Chest

The first postgraduate course in diseases of the chest sponsored by a College chapter was given under the auspices of the Illinois Chapter of the American College of Chest Physicians at the Michael Reese Hospital, Chicago, Illinois, the week of April 1-5, 1946. The following subjects were presented during the six-day course:

### M O N D A Y

#### *Physical Diagnosis*

Ellis B. Freilich, M.D., Associate Professor in Clinical Medicine, University of Illinois College of Medicine.

#### *X-Ray Diagnosis*

Theodore J. Wachowski, M.D., Assistant Professor of Radiology, University of Illinois College of Medicine.

#### *Bronchoscopy*

Paul H. Holinger, M.D., Assistant Professor of Laryngology, Rhinology and Otology, University of Illinois College of Medicine.

#### *Lunch and Round Table Discussion on Practical Application of Above to Hospital, Clinic, Office Practice*

#### *Pneumonias (acute)*

Abraham Feinberg, Lt. Commander, United States Navy.

#### *Post-operative Pulmonary Complications*

William H. Cassels, M.D., Professor of Anesthesia, University of Illinois College of Medicine; Head of Anesthesia Department at Illinois Research and Educational Hospitals.

#### *Traumatic Conditions and Spontaneous Pneumothorax*

Richard H. Meade, Jr., M.D., Formerly Colonel M.C., Kennedy General Hospital, Memphis, Tennessee.

### T U E S D A Y

#### *Fungus Infections*

Isadore Pilot, M.D., Associate Professor of Pathology and Medicine, University of Illinois College of Medicine.

#### *Lung Abscess and Empyema*

Minas Joannides, M.D., Assistant Professor of Surgery, University of Illinois College of Medicine.

#### *Bronchiectasis*

Edwin R. Levine, M.D., Director of Chest Service, Michael Reese Hospital.

#### *Lunch and Round Table Discussion on Non-tuberculous Infections of the Lung*

#### *Bronchogenic Neoplasm*

William E. Adams, M.D., Associate Professor, Department of Surgery, University of Chicago.

#### *Mediastinal Tumors*

Ralph B. Bettman, M.D., Associate Professor of Clinical Surgery, University of Illinois College of Medicine.

#### *Metastatic Tumors*

Erich Uhlmann, M.D., Director of Tumor Clinic, Michael Reese Hospital.

## WEDNESDAY

*Industrial Conditions in Pulmonary Diseases*

Oscar A. Sander, M.D., Studies in Occupational Disease and Industrial Case Findings.

*Emphysema*

Edwin R. Levine, M.D., Director of Chest Service,  
Michael Reese Hospital.

*Pulmonary Decompensation*

Edwin R. Levine, M.D.

*Lunch and Round Table Discussion on Determination of Industrial Relationship to Disease and to Disability**Asthma and Allergic Bronchitis*

Albert H. Andrews, Jr., M.D., Instructor, Department of Otolaryngology, University of Illinois College of Medicine.

*Chemotherapy: Indications and Results*

Italo Volini, M.D., Professor and Head of Department in Medicine, Loyola University College of Medicine; Professor of Internal Medicine, Cook County Hospital and Cook County Graduate School.

*Chemotherapy: Contraindications and Complications*

Italo Volini, M.D.

## THURSDAY

*Pathology and Pathogenesis of Tuberculosis*

Otto Saphir, M.D., Professor of Pathology,  
University of Illinois College of Medicine.

*Epidemiology of Tuberculosis and Control*

Julius B. Novak, M.D., Medical Director,  
Tuberculosis Institute of Chicago and Cook County.

*Primary Tuberculosis and Tuberculosis in Children*

Milton I. Levine, M.D., Assistant Professor in Pediatrics,  
Cornell University Medical College.

*Lunch and Round Table Discussion on Immunity and Vaccination**Diagnosis and Prognosis*

Jay Arthur Myers, M.D., Professor of Preventive Medicine,  
University of Minnesota Medical School.

*Classification of Tuberculosis*

Jay Arthur Myers, M.D.

*Chemotherapy in Tuberculosis*

Karl H. Pfuetze, M.D., Medical Director,  
Mineral Springs Sanatorium.

## FRIDAY

*General Treatment*

Edwin R. Levine, M.D.

*Collapse Therapy (Pneumothorax)*

Minas Joannides, M.D., Assistant Professor of Surgery,  
Illinois University College of Medicine.

*Surgical Collapse*

Richard Davison, M.D., Associate Professor of Surgery,  
Loyola University School of Medicine.

*Lunch and Round Table Discussion on Rehabilitation**Tuberculosis of the E. N. T.*

Francis L. Lederer, M.D., Professor and Head of Department of Laryngology, Rhinology and Otology, University of Illinois College of Medicine.

*Tuberculosis of the Bronchi*

Paul H. Holinger, M.D., Assistant Professor of Laryngology, Rhinology and Otology, University of Illinois College of Medicine.

*G. U. Tuberculosis*

Frederick Lieberthal, M.D., Urologic Staff, University of Illinois College of Medicine.

*Orthopedic Tuberculosis*

Fremont A. Chandler, M.D., Associate Professor of Bone and Joint Surgery, Northwestern University Medical School.

**S A T U R D A Y***Discussion on Differential Diagnosis*

Twenty-five physicians from 17 states and the Philippine Islands registered for the course. On Friday night, April 5, a dinner was given for the instructors and for the physicians who registered for the course. Dr. Fred M. F. Meixner, Peoria, Illinois, President of the Illinois Chapter of the College, presided and kept the audience entertained with stories from his large repertoire of rare wit. Dr. Samuel Soskin, Director of Postgraduate Medical Education at Michael Reese Hospital, addressed the guests and Dr. Hubert A. Boyle, Middleton, Massachusetts, class valedictorian, presented the following message:

"I have been selected by the physicians from 17 states and the Philippine Islands, to say a few words of appreciation to our instructors concerning the postgraduate course on diseases of the chest which has just been concluded here in Chicago. We are deeply grateful to the doctors who have given so unselfishly of their time and energy to give us this very interesting course. All of us are happy to have had the opportunity to listen to these eminent teachers and to have been able to participate in this most instructive course on diseases of the chest.

"We especially want to extend our thanks to Dr. Edwin R. Levine, Chairman of the medical education committee of the Illinois Chapter of the American College of Chest Physicians, for his untiring efforts in organizing and directing this course. We also wish to thank the management of the Michael Reese Hospital for their hospitality.

"With each of our instructors we wish to leave a sincere note of appreciation for the knowledge which has so generously been given to us in the lecture room.

"We understand that this is the first class to have had the privilege of taking a postgraduate course in diseases of the chest under the auspices of the Illinois Chapter of the American College of Chest Physicians and we are deeply honored to be members of the class of 1946. It is our sincere hope that the course will be repeated annually and that those who follow us will profit as much from the succeeding courses as we have profited from this one. We again want to thank you for your cordial hospitality and we shall never forget the many happy days spent in your city."

Registration fee for the course was \$50.00.

## Editorial

### TUBERCULOSIS IN HOSPITAL PERSONNEL

In this issue Dr. Alarcon presents the results of observations on 357 sanatorium employees who were in intimate contact with patients for variable periods of time, ranging from several weeks to eight years. All employees were over twenty years of age and had primary tuberculous lesions as manifested by the tuberculin reaction when employed. They were carefully instructed to protect themselves against contamination with tubercle bacilli.

During the period of observation only four (1.1 per cent) developed x-ray evidence of lesions thought to be tuberculous which were not demonstrable at the time employment began. This report strongly supports the contention of a number of workers, that most of the lesions reported to have promptly developed among persons who became reactors to tuberculin on tuberculosis services in various parts of the world were only of the primary type and its immediate sequelae such as pleuritis. Therefore they should not be confused with lesions of the chronic reinfection type. For example, in 1936 Heimbeck reported that among 280 students of nursing who became reactors to tuberculin while under his observation, 96 developed tuberculosis. However, on analysis one finds that 39 had erythema nodosum and another 26 only pulmonary infections, which we assume were primary infiltrates. In 16 others there was only evidence of pleuritis. Two others had tuberculous meningitis, and the remaining 13 developed pulmonary lesions which at the time were thought to represent the reinfection type of disease.

For twenty years we have studied tuberculosis among students of nursing and medicine who entered school as tuberculin reactors, as well as those who became reactors under our observation. For example, among 160 medical students who entered as tuberculin reactors, 3.1 per cent developed reinfection type of lesions while in school or soon after graduation; whereas among 145 who became reactors while in school, 9.6 per cent developed demonstrable lesions. This statement might be interpreted to mean that more than three times as many students who became reactors while in school developed clinical tuberculosis as among those who entered as reactors. Actually, however, this is not true. In fact, of the 9.6 per cent in whom demonstrable lesions were seen, primary complexes and pleurisy accounted for 6.2 per cent; whereas only 3.4 per cent developed chronic reinfection type of tuberculosis, and even some of those lesions later proved to be only the primary type. Thus, only the 3.4 per cent are comparable

with the 3.1 per cent who developed clinical lesions among the students who entered as reactors.

Among student nurses we reported 281 who entered school as tuberculin reactors and 3.6 per cent later developed reinfection type of disease. Lesions were demonstrated in 9.8 per cent of 419 students who became infected while in school. However, of the 9.8 per cent, 5.3 per cent had only demonstrable primary infiltrates or pleuritis, and the remaining 4.5 per cent was reported as having probable to definite clinical lesions. Later reports will show that some of the 4.5 per cent were eventually found to be primary infiltrates.

The statement so often made that far more cases of tuberculosis develop among those who become infected while in school than among those infected before entering school is based on comparing unlike conditions. Primary parenchymal lesions, pleurisy with effusion, erythema nodosum and the reinfection chronic types of lesions which appear among those recently infected are grouped and compared with only the chronic reinfection type of lesions which develop among those long since infected. Among our entire group of students of nursing and medicine we have been unable to find any significant difference in the development of the chronic reinfection type of tuberculosis among those entering as reactors and those who become reactors while in school.

All of our students, as well as those reported by Heimbeck who entered as reactors, already had primary tuberculous lesions in their bodies. These students and the group from which they were drawn had already undergone what those who became reactors after entering school experienced while under observation. Likewise, all of those who became reactors while in school developed primary lesions, but only in a small percentage of them were the lesions so situated or attained sufficient size or density to have their locations determined by our crude methods of examining the living body.

Dr. Alarcon's 357 employees had primary tuberculosis and their tissues were sensitized to tuberculo-protein at the beginning of their service. Inasmuch as 80 per cent had x-ray evidence of the disease at the time, such as residual primary lesions and local fibrosis from old reinfections, they obviously would not develop primary infiltrates, little or no erythema nodosum or pleurisy with effusion, associated with fresh primary lesions. Although an attempt was made to protect the employees against the patients' tubercle bacilli, evidently strict contagious disease technique was not employed. Therefore it is probable that patients' tubercle bacilli did enter the bodies of some of the employees. Any infections that occurred in this manner would of necessity be reinfec-

tions, and lesions so produced are notoriously slow in their development. Long ago Krause and others pointed out that when tubercle bacilli are implanted on allergic tissues, an immediate specific reaction occurs which fixes them at the point of lodgment. However, the tubercle bacilli are not destroyed, and they may produce lesions which evolve so slowly that they are not demonstrable for many months or years.

The problem of endogenous reinfection is also involved in Dr. Alarcon's employees. He does not state how long or how many were exposed only for several weeks or how many for intervening periods up to eight years. Among 357 adults with primary tuberculosis one would expect several to develop lesions from endogenous reinfection as the years pass, even though they were not reinfected exogenously while employed in the sanatorium. If these individuals can be followed for twenty more years or longer, Dr. Alarcon will then be able to make another significant contribution to our knowledge of tuberculosis. The important consideration is not whether those who enter as reactors or those who become reactors while working with patients develop more tuberculosis, but how to prevent all persons from becoming infected and reinfected with tubercle bacilli.

J. A. M.

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## College Chapter News

### MISSOURI CHAPTER

The annual meeting of the Missouri Chapter, American College of Chest Physicians, was held at the Jefferson Hotel, St. Louis, Missouri, March 24-25. The Chapter luncheon meeting was addressed by Dr. Jay Arthur Myers, Minneapolis, Minnesota, President of the College. At a round table discussion presented before the meeting of the Missouri State Medical Society, and presided over by Dr. H. I. Spector, Regent of the College for the district, Drs. Ralph A. Kinsella, Evarts A. Graham, James L. Mudd, LeRoy Sante and Jay Arthur Myers participated. Over 500 physicians attended this session. The following officers were elected:

Samuel Harrison Snider, M.D., Kansas City, *President*.  
William W. Buckingham, M.D., Kansas City, *Vice-President*.  
Alexander Steiner, M.D., St. Louis, *Secretary-Treasurer*.

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### MARYLAND - DISTRICT OF COLUMBIA CHAPTER

A new chapter of the College was organized at Baltimore, Maryland on April 22nd comprising Maryland, the District of Columbia, and West Virginia. A scientific session was presented which was followed by an x-ray conference. Dr. Otto C. Brantigan, Baltimore, Maryland, was in charge of the arrangements for the meeting and Dr. Bartus T. Baggott, Baltimore, Maryland, was chairman of the X-ray Conference. Dr. J. Winthrop Peabody, Washington, D. C., past-president of the College, was guest speaker at the dinner meeting. The following officers were elected:

William F. Rienhoff Jr., M.D., Baltimore, Maryland, *President*.  
William LeRoy Dunn, M.D., Washington, D. C., *Vice-President*.  
I. B. Lyon, M.D., State Sanatorium, Maryland, *Secretary-Treasurer*.

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### NORTH MIDWEST CHAPTER

The North Midwest Chapter, American College of Chest Physicians, met in conjunction with the Iowa State Medical Society at Des Moines, on April 18th. A scientific program was presented and the following officers were re-elected:

J. Carl Painter, M.D., Dubuque, Iowa, *President*.  
John F. Allen, M.D., Omaha, Nebraska, *Vice-President*.  
Karl H. Pfuetze, M.D., Cannon Falls, Minnesota, *Secretary-Treasurer*.

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### NEW YORK STATE CHAPTER

The New York State Chapter, American College of Chest Physicians, met in conjunction with the New York State Medical Society at New York City on May 2nd. A scientific program on diseases of the chest was presented. The following officers were elected:

Samuel A. Thompson, M.D., New York City, *President*.  
Foster Murray, M.D., Brooklyn, *First Vice-President*.  
Grant Thorburn, M.D., New York City, *Second Vice-President*.  
Donald R. McKay, M.D., Buffalo, *Secretary-Treasurer*.

The following appointments have been made for 1946-1947:

*Program Committee:*

James S. Edlin, M.D., New York City, *Chairman*  
Nelson W. Strohm, M.D., Buffalo  
George Foster Herben, M.D., Yonkers  
David Ulmer, M.D., New York City

*Medical Education Committee:*

George Ornstein, M.D., New York City, *Chairman*  
Charles E. Hamilton, M.D., Brooklyn  
Abel Levitt, M.D., Buffalo  
Reuben J. Erickson, M.D., Albany  
James L. Mangano, M.D., Rochester  
Edward P. Eglee, M.D., New York City  
Edgar Mayer, M.D., New York City

*Membership Committee:*

Grant Thorburn, M.D., New York City, *Chairman*  
Charles C. Trembley, M.D., Saranac Lake  
Arthur Q. Penta, M.D., Schenectady  
Fred W. Holcomb, M.D., Kingston  
I. D. Bobrowitz, M.D., Otisville  
Sidney A. Britten, M.D., Syracuse  
George C. Adie, M.D., New Rochelle.

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## ILLINOIS CHAPTER

The Illinois Chapter, American College of Chest Physicians, met in conjunction with the Illinois State Medical Society at Chicago, Illinois on May 13th. A scientific program on chest diseases was presented. Dr. H. I. Spector, St. Louis, Missouri, Regent of the College, was the guest speaker at the dinner. The following officers were elected:

Julius B. Novak, M.D., Chicago, *President*  
Arthur S. Webb, M.D., Glen Ellyn, *Vice-President*  
Kenneth G. Bulley, M.D., Aurora, *Secretary-Treasurer*

The following appointments were made for 1946-1947:

*Program Committee:*

Darrell Trumpe, M.D., Springfield, *Chairman*  
Kenneth G. Bulley, M.D., Aurora  
David Loewen, M.D., Decatur

*Medical Education Committee:*

Edwin R. Levine, M.D., Chicago, *Chairman*  
Paul H. Holinger, M.D., Chicago  
Minas Joannides, M.D., Chicago

*Membership Committee:*

Fred M. F. Meixner, M.D., Peoria, *Chairman*  
Richard Davison, M.D., Chicago  
Otto C. Schlack, M.D., Oak Forest

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## TEXAS CHAPTER

The annual meeting of the Texas Chapter, American College of Chest Physicians, was held in conjunction with the Texas State Medical Society at Galveston, Texas, on May 6th. A scientific program was presented and the following officers were elected:

Robert G. McCorkle, M.D., San Antonio, *President*  
H. Frank Carman, M.D., Dallas, *First Vice-President*  
Robert B. Homan, M.D., El Paso, *Second Vice-President*  
Elliott Mendenhall, M.D., Dallas, *Secretary-Treasurer*

The following committees have been appointed:

*Program Committee:*

Charles J. Koerth, M.D., Kerrville, *Chairman*  
J. Emerson Dailey, M.D., Houston  
Henry R. Hoskins, M.D., San Antonio

*Medical Education Committee*

Thomas R. Jones, M.D., Houston, *Chairman*  
H. Frank Carman, M.D., Dallas  
George S. McReynolds Jr., M.D., Galveston

*Public Relations Committee:*

W. D. Anderson, M.D., San Angelo, *Chairman*  
Walter C. Brown, M.D., Corpus Christi  
Wayne A. Reser, M.D., Wichita Falls

*Membership Committee:*

William W. Coulter Jr., M.D., Sanatorium, *Chairman*  
John S. Chapman, M.D., Dallas  
John Roberts Phillips, M.D., Houston  
Robert W. Taylor, M.D., Lufkin  
Jesse B. White, M.D., Amarillo

*Nominating Committee*

Charles M. Hendricks, M.D., El Paso, *Chairman*  
Sim Hulsey, M.D., Fort Worth  
Howard E. Smith, M.D., Austin

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#### NEW JERSEY CHAPTER

The New Jersey Chapter, American College of Chest Physicians, met in conjunction with the New Jersey State Medical Society at Atlantic City on May 21st. A scientific program was presented and the following officers were elected for the chapter:

Irving Willner, M.D., Newark, *President*  
Harold S. Hatch, M.D., Morristown, *Vice-President*  
Paul K. Bornstein, M.D., Asbury Park, *Secretary-Treasurer*

Committee appointments for 1946-1947 have been made as follows:

*Program Committee:*

Irving L. Applebaum, M.D., Newark, *Chairman*  
Homer H. Cherry, M.D., Paterson  
Anthony Crecca, M.D., Newark

*Medical Education Committee:*

Richard Dieffenbach, M.D., Newark, *Chairman*  
William Wakeley, M.D., Orange  
William L. Weintraub, M.D., Paterson

*Membership Committee:*

Harold S. Hatch, M.D., Morristown, *Chairman*  
Allan J. Stolow, M.D., Hackettstown  
Clyde M. Fish, M.D., Pleasantville  
Emanuel Klosk, M.D., Newark

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#### ARIZONA CHAPTER

The Arizona Chapter, American College of Chest Physicians, met in conjunction with the Arizona State Medical Society at Phoenix on May 1st. A scientific program was presented and the following officers were elected:

Charles A. Thomas, M.D., Tucson, *President*  
Bertram Snyder, M.D., Phoenix, *Vice-President*  
Leslie B. Smith, M.D., Phoenix, *Secretary-Treasurer*

This chapter was originally the Southwestern States Chapter and has been re-organized as the Arizona Chapter of the College.

## OHIO CHAPTER

The Ohio Chapter, American College of Chest Physicians, met in conjunction with the Ohio State Medical Society at Columbus on May 8th. A scientific program was presented and the following officers were elected:

Elmer E. Kirkwood, M.D., Youngstown, *President*  
Irville S. Rian, M.D., Mt. Vernon, *Vice-President*  
William A. Potts, M.D., Columbus, *Secretary-Treasurer*

## PENNSYLVANIA CHAPTER

The Pennsylvania Chapter, American College of Chest Physicians, met in conjunction with the Laennec Society of Philadelphia, on April 3, at Philadelphia. A scientific program was presented and the following officers were elected:

Chevalier L. Jackson, M.D., Philadelphia, *President*  
Henry A. Gorman, M.D., Hamburg, *Vice-President*  
Edward Lebovitz, M.D., Pittsburgh, *Secretary-Treasurer*

## NORTH BRAZILIAN CHAPTER TO BE ORGANIZED

The North Brazilian Chapter of the American College of Chest Physicians will be formally organized during the meeting of the Third Brazilian Tuberculosis Congress at Sao Salvador, Bahia, October 6-12, 1946. The Brazilian Institute for Tuberculosis Research (I.B.I.T.) which was dedicated on February 21st with fitting ceremonies will house the North Brazilian Chapter of the College (Fig. 1). The organization of this new College Chapter is due to the untiring efforts of Dr. Jose Silveira, Director of the Institute and Governor of the College for the North Brazilian States. The new chapter will comprise the College members in all of the Brazilian States north of Minas Geraes. The fol-



*The Brazilian Institute for Tuberculosis Research (I.B.I.T.)  
Sao Salvador, Bahia*

lowing College members residing in the district will be enrolled as Charter Members of the North Brazilian Chapter:

*Alagoas* (Maceio)

\*Lourival de Mello Motta, M.D., F.C.C.P.

*Bahia* (Salvador)

Mario Macedo Costa, M.D.

\*Cesar de Araujo, M.D., F.C.C.P.

\*Manoel Ezequiel da Costa, M.D., F.C.C.P.

Jose F. de Figueiredo, M.D.

Moacyr Siewas de Goes, M.D.

Carlos Rodrigues de Moraes, M.D.

Aloysio Durval, M.D.

Luis Tarquinio Pontes, M.D.

Humberto Raimundo Valente Peixoto, M.D.

\*Adelaido Ribeiro, M.D., F.C.C.P.

Francisco dos Santos Serra, M.D.

\*Jose Silveira, M.D., F.C.C.P.

Itazil Benicio dos Santos, M.D.

Jose Coelho dos Santos, M.D.

Jaime Pontes Tanajura, M.D.

*Ceara* (Fortaleza)

Rafael de Codes y Sandoval, M.D.

Joao Otavio Lobo, M.D.

*Para* (Belem)

Epilogo de Campos, M.D.

*Pernambuco* (Recife)

Miguel do Nascimento Arcanjo, M.D.

Joaquim S. Cavalcanti, M.D.

Otavio de Freitas, M.D.

Agenor de Sousa Bomfim, M.D.

Vicente Ferreira Pinzon, M.D.

*Rio Grande do Norte* (Natal)

Carlos Alberto Passos, M.D.

\*Fellows.



*View of the Auditorium and Lecture Hall*

*South Brazilian Chapter*

The Brazilian Chapter for the Southern States, to include the Federal District of Rio de Janeiro, will continue to function under the direction of the present officials of the Chapter. These officers are:

Samuel Libanio, M.D., Rio de Janeiro, *President*  
 Galdino Travassos, M.D., Rio de Janeiro, *Vice-President*  
 Jose Carvalho Ferreira, M.D., Rio de Janeiro, *Executive Secretary*  
 Affonso MacDowell Filho, M.D., Rio de Janeiro, *Secretary-Treasurer*

The members of this Chapter are:

*Parana (Lapa)*

Abrahaao Serebrenick, M.D.

*Rio de Janeiro, D. F.*

\*Aresky Amorin, M.D., F.C.C.P.  
 Luis Arontes de Almeida, M.D.  
 Marcio Bueno, M.D.  
 Joao Martins Castello Branco, M.D.  
 \*Reginaldo Fernandes, M.D., F.C.C.P.  
 Jose Carvalho Ferreira, M.D.  
 Olimpio Gomes, M.D.  
 Henri Eugene Jouval, M.D.  
 \*Samuel Libanio, M.D., F.C.C.P.  
 \*Affonso MacDowell, M.D., F.C.C.P.  
 Affonso MacDowell Filho, M.D.  
 Paulo Marchese, M.D.  
 Roberto Pereira, M.D.  
 Galdino Travassos, M.D.

*Est. do Rio (Niteroy)*

Joao da Silva Vizella, M.D.

*Rio Grande do Sul (Porto Alegre)*

Gaspar Faria, M.D.

*Sao Paulo (Marilia)*

J. Coriolano de Carvalho, M.D.

*Sao Paulo (Sao Paulo)*

\*Clemente Ferreira, M.D., F.C.C.P.

*Espirito Santo (Victoria)*

Jaime dos Santos Neves, M.D.

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*\*Fellows.*

Dr. Affonso MacDowell, Rio de Janeiro, Director of the Journal, "Revista Brasileira de Tuberculose" is the Regent of the College for the country.

The following program is to be presented at the Third Brazilian Tuberculosis Congress:

1. "Padronisacao das tecnicas de Laboratorio aplicaveis a Clinica da tuberculose e a Vacinacao B. C. G."  
     Arlindo de Assis, M.D., Rio de Janeiro, Brazil.
2. "Aspectos clinicos da tuberculose da criancas no Brasil."  
     Rafael de Paula Sousa, M.D.
3. "Diagnostico e terapeutica precoces como base da campanha anti-tuberculosa."  
     Jose Silveira, M.D., Bahia, Brazil.

The Congress will be conducted under the auspices of the following officials:

Cesar de Araujo, M.D., *President*

Jose Silveira, M.D., *Vice-President*

Francisco Serra, M.D., Almeida Gouveia, M.D., y

Jose Figueiredo, *Secretaries*.

## ARGENTINA CHAPTER

The Argentina Chapter of the American College of Chest Physicians will meet on July 13 in Alta Gracia (Cordoba Province). The meeting will be given as a testimonial to honor the memory of Dr. Ralph C. Matson, former Editor of "Diseases of the Chest".

The subject "Technique and Interpretation of the Results of the Investigation of the Tuberculin Allergy in Collectivities," will be discussed by Professors Raul F. Vaccarezza, Justo Lopez Bonilla, and Jose Antonio Perez. There will be a luncheon and an election of officers for the chapter.

Juan Carlos Rey, M.D., *Secretary-Treasurer*.

## GREEK CHAPTER

The Greek Chapter of the American College of Chest Physicians was organized at Athens, Greece on March 18 and the following officers were elected:

Nicholas Oekonomopoulos, M.D., Athens, *President*  
Basil Papanicolaou, M.D., Athens, *Vice-President*  
Eugene Joannides, M.D., Athens, *Secretary-Treasurer*

Dr. Nicholas Oekonomopoulos, President of the Chapter, was appointed as Regent of the College for Greece, and Dr. Basil Papanicolaou, Vice-President of the Chapter, was appointed as Governor.

Under Dr. J. B. McDougall, Chief of the Greece Mission, Tuberculosis Section of UNRRA, the mass radiology center was opened at Salonica, Greece on April 18. Mass radiology was first inaugurated by the mission's health division in Athens six months ago. It is planned to examine 100,000 subjects during 1946, giving Greek medical authorities reliable data on the incidence of tuberculosis which apparently doubled during the war and occupation. Of these, 26,000 persons have been x-rayed in Athens, other thousands will be tested in Salonica and a third center will shortly go into operation at Patras.

## College News Notes

## MAJOR BEATTY CITED

The Bronze Star medal was awarded to Major Gerald A. Beatty, Medical Corps, U. S. Army, a Fellow of the College, from Wilmington, Delaware, for meritorious service in support of combat operations from March 22, 1945 to May 8, 1945 in France and Germany. The citation was recently received by Major Beatty who is now on terminal leave.

Major Beatty served with the Third Hospitalization Unit, Tenth Field Hospital. He entered the service in July 1942, and spent two and a half years overseas. In that time he saw service in the Middle East, North Africa, Italy, France and Germany. He returned to this country in July 1945.

His citation read in part: "Maj. Beatty's energy, cooperative spirit, foresight and knowledge made it possible to support rapidly moving combat troops. At all times his exemplary devotion was inspirational to both patients and personnel of the unit."

## COLLEGE FELLOWS JOIN VETERANS ADMINISTRATION

Dr. Benjamin L. Brock, F.C.C.P., Waverly Hills, Kentucky has resigned as Medical Director of the Waverly Hills Sanatorium and Tuberculosis Controller of the city of Louisville and Jefferson County, Kentucky to accept a position with the Veterans Administration as Clinical Director of its largest tuberculosis hospital at Oteen, North Carolina. Dr. Brock has been Associate Professor of Medicine at the University of Louisville School of Medicine since 1938 and has made a number of contributions to the literature on tuberculosis. He is a veteran of the World War; Fellow of the American College of Physicians; Fellow of the American College of Chest Physicians and a member of the American Medical Association.

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Dr. Edgar C. Harper, F.C.C.P., Richmond, Virginia, has accepted an appointment in the new Department of Medicine and Surgery. He will assume the duties of Assistant Chief of the Tuberculosis Division at the Veterans Administration Branch Office No. 4 in Richmond, Virginia.

Dr. Harper is a veteran of World War I. After his separation from active duty with the U. S. Army, he served as Resident in Tuberculosis at the Catawba Sanatorium, Catawba, Virginia. He then engaged in private practice, confining his practice to tuberculosis and diseases of the chest and served as Visiting Physician at the Johnston-Willis Hospital in Richmond, Virginia. Prior to his appointment in the Department of Medicine and Surgery of the Veterans Administration, Dr. Harper was Director of the Tuberculosis Field Service of the Virginia State Health Department and was an Instructor in Physical Diagnosis and Special Lecturer on Tuberculosis at the Medical College of Virginia in Richmond, Virginia.

Dr. Harper is a Fellow of the American College of Chest Physicians and a member of the American Medical Association, the American Public Health Association and the Richmond, Virginia, Academy of Medicine.

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Dr. Russell H. Frost, F.C.C.P., Owatonna, Minnesota, has accepted an appointment in the new Department of Medicine and Surgery of the Veterans Administration. He will assume the duties of Assistant Chief, Tuberculosis Division, Branch Office No. 8, Minneapolis, Minnesota.

Dr. Frost is a veteran of World War II, having served on active duty in the U. S. Navy. Before entering into active naval duty, he had served as Medical Director, G. B. Cooley Sanatorium, Monroe, Louisiana, and was on the Attending Staff of St. Francis Sanatorium and the Monroe State Charity Hospital, Monroe, Louisiana. Prior to that he had served as Medical Director and Superintendent of the Buena Vista Sanatorium, Wabasha, Minnesota, and as Senior Resident Physician, Glen Lake Sanatorium, Oak Terrace, Minnesota. He also was Assistant in cardiology and internal medicine, St. Paul Clinic, St. Paul, Minnesota, and was a resident in medicine at the Abbott Hospital, Minneapolis, Minnesota.

Dr. Frost is a Fellow of the American College of Chest Physicians and of the American Medical Association. He is a member of the Quachita Parish Medical Society, Monroe, Louisiana.

Dr. Harry Leon Katz, F.C.C.P., New York City, New York, has accepted an appointment in the new Department of Medicine and Surgery. He will assume the duties of Assistant Chief, Tuberculosis Division, Branch Office No. 2, New York, New York.

Dr. Katz is a veteran of World War II; having served on active duty with the U. S. Army, during which time he was assigned as Chief of Chest Service at the Tilton General Hospital, Fort Dix, New Jersey. Prior to entering the military service, Dr. Katz served a residency in tuberculosis at Sea View Hospital, New York City, New York, and has been Instructor in Physiology at Ohio State University, Columbus, Ohio.

Dr. Katz is a Fellow of the American College of Chest Physicians and a member of the American Medical Association.

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Dr. Charles J. Kaufman, F.C.C.P., Denver, Colorado, has accepted an appointment in the Department of Medicine and Surgery of the Veterans Administration. He has assumed the duties of Chief of Section, Tuberculosis, Veterans Administration Hospital, Castle Point, New York.

Prior to accepting this appointment, Dr. Kaufman was Associate Professor of Medicine at the University of Colorado School of Medicine and served as Medical Director of the National Jewish Hospital at Denver, Colorado. He was formerly an Instructor in Clinical Medicine at Cornell University Medical College, and Assistant Physician and then Physician at the Metropolitan Hospital, New York City. He also served as Attending Physician at Sea View Hospital, Staten Island, New York, and was engaged for a time in private practice, specializing in tuberculosis and internal medicine. He spent some time as a Fellow in Experimental Research at Trudeau Laboratory, Saranac Lake, New York, and was also Resident Physician at Northwood Sanatorium and Resident in Tuberculosis at the Eagleville Sanatorium, Eagleville, Pennsylvania.

Dr. Kaufman is a Fellow of the American College of Chest Physicians and a member of the American Medical Association.

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Major H. Charles Schock, Cleveland, Ohio, recently received the Army Commendation Award "for meritorious service as Chief of Officer's Tuberculosis Section, Medical Service, Fitzsimons General Hospital, Denver, Colorado. He, through his ability and unstinting efforts, and in spite of inadequate and constantly changing personnel, supervised a service of superior professional effectiveness to the great benefit of patients at that hospital." Dr. Schock, a Fellow of the American College of Chest Physicians, graduated from Western Reserve University, Cleveland, in 1927, and entered the service in September, 1942.

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Dr. F. R. Ferlaino, New York City, participated in a symposium on industrial medicine presented by the New York Post-Graduate Medical School, Columbia University, New York City, June 10-14, 1946. Dr. Ferlaino discussed "Upper respiratory tract infections. The common cold: its prevention and methods of treatment," "Causes of industrial absenteeism and remedies," and "Use of penicillin in industry".

Dr. Robert Neubauer of Yugoslavia was elected a Fellow of the American College of Chest Physicians. Dr. Neubauer is well trained in chest diseases and recently headed a Red Cross Mission from Yugoslavia to the United States.

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A scientific program on chest diseases was presented at the 93rd annual session of the Minnesota State Medical Society under the auspices of the American College of Chest Physicians. The following program was given:

- "Diseases of the Esophagus," Herbert W. Schmidt, M.D., Rochester.
- "The Importance of Isolation of all Positive Cases of Tuberculosis," Bernard J. Terrell, Nopeming.
- "Modern Treatment of Empyema," Thomas J. Kinsella, Minneapolis.
- "The Accuracy of Cultures of Pulmonary Secretions in Evaluating Activity in Pulmonary Tuberculosis," L. I. Sanford, M.D., Milwaukee, Wisconsin.

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The Argentine Society of Bronchoesophagology elected the following officers at their annual meeting held at Buenos Aires on March 29th:

- President:* Dr. Alvaro E. Bence
- Vice-President:* Dr. Antonio Carrascosa
- Secretary:* Dr. Horacio Resano
- Assistant Secretary:* Dr. Ricardo Bisi
- Treasurer:* Dr. Jorge Taiana
- Assistant Treasurer:* Dr. Mario Brea
- Directors:* Dr. Abelardo Irigoyen Freire (Santa Fe)  
Dr. Renato Segre  
Dr. Jose Ameriso (Rosario)  
Dr. Mario Rius (Montevideo)

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Dr. J. H. Blackburn, Regent of the College for Australia, was appointed a corresponding member of the Tuberculosis Association of India.

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Dr. Alvin B. Mullen, Waverly Hills, Kentucky, has been appointed Medical Director of Waverly Hills Sanatorium to succeed Dr. Benjamin L. Brock. Dr. Mullen was formerly a Resident Physician at Waverly Hills until entering the Armed Forces in 1942. He served as Chief of Medical Service of the 316th Station Hospital in England and Scotland and later as Commanding Officer of the unit.

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## Obituaries

### ALEXANDER WILLIAM ADAMSKI

1911 - 1946

Dr. Alexander William Adamski of Racine, Wisconsin, died instantly of a self-inflicted gunshot wound January 3, 1946. He was the assistant surgeon at Sunny Rest Sanatorium for the past two years.

Dr. Adamski graduated from the Marquette University Medical School in 1934 and served his internship in Brooklyn, New York. He came to Racine and was in practice since 1935. He enjoyed a large practice and was recognized as a very successful physician. Among his accomplishments was a new technique for blood transfusions in infants. This subject was published recently in the Wisconsin Medical Journal. It attracted much attention.

Besides his membership in the American College of Chest Physicians Dr. Adamski was active in the Racine County Medical Society, the Wisconsin State Medical Society, and the American Medical Association. He was a member of St. Mary's Hospital Staff and held several appointments with industrial concerns and fraternal orders.

Carl O. Schaefer, M.D., *Governor for Wisconsin.*

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### OSBOURNE O. ASHWORTH

1895 - 1945

It is with deep sorrow that the American College of Chest Physicians records the passing of a distinguished and valuable member. Be it resolved that the American College of Chest Physicians has lost a valuable member, the medical profession a brilliant physician and a host of loyal patients a friendly counsellor.

Dr. Ashworth was born in Ashboro, North Carolina on August 2, 1895. He was one of a large family and early in life came to Richmond in search of an education which he obtained in the Richmond Academy, Richmond College, and the Medical College of Virginia where he graduated in 1921. He interned in Saint Elizabeth Hospital and continued his studies at Catawba Sanatorium and the Mayo Clinic.

When he began practicing in Richmond he developed a large clientele of chest cases. He was amongst the first in the state to emphasize the importance of collapse therapy in the treatment of the tuberculous. Although he was seriously handicapped by physical ailment, he continued actively and energetically in the practice of medicine until his untimely death.

Be it further resolved that these resolutions be spread upon the minutes of the American College of Chest Physicians.

Dean B. Cole, M.D., *Governor for Virginia.*

**TUBERCULOSIS CONTROL DIVISION RELEASES NEW FILMS***Two New Films Available on Administration of Mass Radiography Programs*

Two motion pictures on tuberculosis case-finding with miniature film mass radiography of the chest have just been completed for the U. S. Public Health Service, under the supervision of the Tuberculosis Control Division. The films demonstrate the techniques, the staff, procedures and equipment required for: (1) routine admission miniature film chest x-ray examination of all patients and personnel entering general hospitals; (2) miniature film mass radiography in community tuberculosis case-finding programs.

These are teaching and orientation films for an audience of professional, technical, or administrative personnel, or trainees, in the fields of medicine, public health, and hospital care. The film prints are 16 mm. size, black and white, with sound.

*Routine Admission Chest X-Ray in General Hospitals*

This film was photographed at University hospital, Ann Arbor, Michigan. After an introductory statement about mass radiography by Dr. Fred J. Hodges, Professor, Department of Roentgenology, the film shows the step-by-step sequence of routine miniature film chest x-ray service for all patients admitted to the hospital or clinic. Case histories are re-enacted and the corresponding x-ray films shown, to demonstrate the efficiency and benefits of this service. Animated drawings are used to illustrate the operation of the phototimer, to present case-finding statistics, and to demonstrate the physical arrangement of the admission chest x-ray unit. Details of record keeping, of film processing, interpretation, reporting, and filing are presented. The film demonstrates the danger of undiagnosed tuberculosis in hospitals. It highlights the benefits of early diagnosis for treatment of non-tuberculous as well as tuberculous pathology found in hospital patients as a group, when all receive routine chest x-ray examination. The compactness, simplicity, speed and efficiency of miniature film chest x-ray equipment are shown. Throughout the film are many scenes demonstrating the advantages, benefits, and practicability of miniature film x-ray equipment and routine admission chest x-ray service.

*Techniques of Group Chest X-Ray Services*

This film provides community health leaders and public health personnel with an up-to-date and detailed procedure outline for administration and operation of miniature film mass radiography case-finding programs. It features the basic and the newest developments in equipment and techniques. The film re-enacts a conference attended by representatives of official and voluntary health agencies, professional groups, labor and management, and then illustrates the functions and responsibilities of each—before, during, and following a typical mass radiography project. The second half of the film depicts an actual mass radiography project in operation—from the time it is first planned and scheduled, until it is completed and all reports tabulated. The major theme is the importance of organization, planning, and teamwork. Photography and narration highlight all the details that must be carefully considered by the responsible administrative group and by the operating personnel.

*Loan and Purchase Data:* After July 1, 1946, a print of each film will be available for short-term loan from Tuberculosis Control Division Consultants in the District Offices of the U. S. Public Health Service. Prints may be purchased from Castle Films, Inc., 30 Rockefeller Plaza, New York 20, New York.

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| <i>Routine Admission Chest X-Ray in General Hospitals</i> | \$23.00 per print |
| <i>Techniques of Group Chest X-Ray Services</i>           | \$21.00 per print |

### C. S. C. ANNOUNCES CRYSTALLINE SODIUM PENICILLIN

The commercial production of sodium penicillin in crystalline form was announced March 26th by Commercial Solvents Corporation. Of unusually high potency, this crystalline preparation is heat stable, eliminating the need for refrigeration. Hence, crystalline penicillin may be carried in the physician's emergency bag without loss in potency.

This significant advance in penicillin therapy is made possible by the introduction of special crystallization processes in the final production stages of the sodium salt of penicillin, heretofore manufactured as an amorphous material.

The potency of this new crystalline form of penicillin ranges from 1,400 to 1,500 units per mg. Because of its heat stability, crystalline penicillin is more easily stored in hospitals and pharmacies at room temperature, and many transportation problems are avoided.

Crystalline sodium penicillin is white in color and odorless. Under the microscope the crystals are readily visible. The crystalline nature is also shown by x-ray diffraction patterns.

Clinically, crystalline sodium penicillin offers distinct advantages. It permits larger doses in the aerosol treatment of upper respiratory infections; doses as high as 200,000 units each are well tolerated with this high-potency material. In meningeal infections, larger doses are tolerated in the subarachnoid space without evidence of nervous system irritation. The material also may be injected subcutaneously—instead of intramuscularly—without the discomfort formerly attendant upon the injection of lower-potency materials. In intramuscular injection, the same advantage accrues.

In line with a recently announced policy, all vials of crystalline sodium penicillin—C. S. C. will carry a statement of the potency per mg. on the label of each vial enabling the physician to know at a glance the degree of purification achieved. Within short order, all penicillin manufactured by Commercial Solvents Corporation will be Penicillin-C. S. C. Crystalline Sodium Salt, and will be packaged in vials of 100,000 units, 200,000 units, and 500,000 units, respectively.

### ANNOUNCEMENT

As this issue of the journal goes to press, the College will be holding its Twelfth Annual Meeting at San Francisco, California, June 27-30, 1946. A complete report of the proceedings of the meeting will be published in future issues of *Diseases of the Chest*.

## Positions Wanted and Available

### POSITIONS AVAILABLE

Physician interested in sanatorium work, position available in 200-bed state sanatorium in middle west. Will meet reasonable demands for salary. For further information please address Box 141A, American College of Chest Physicians, 500 N. Dearborn St., Chicago 10, Illinois.

Positions available for resident physicians in 500 bed sanatorium. Experience in tuberculosis work and interest in research desirable. For further particulars please address Box 140A, American College of Chest Physicians, 500 N. Dearborn Street, Chicago 10, Illinois.

Wanted: Assistant Physician for tuberculosis sanatorium (Massachusetts). Must be graduate Class A school with some experience in tuberculosis. State age, professional history and other details first letter. Please address Box 138A, American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois.

Positions open in state department of public health. Physicians wanted who have had three years of experience in full time tuberculosis work, or with one year of experience in tuberculosis work and the rest in full time public health work. Salary \$5,640 per annum, plus expenses of official travel, transportation, board and lodging. For further information please address Box 139A, American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois.

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### POSITIONS WANTED

Well trained chest physician, to be released from service, would like to become associated with physician in private practice, clinic or sanatorium. Preferably in California. For further information please address Box 226A, American College of Chest Physicians, 500 North Dearborn St., Chicago 10, Illinois.

Physician, 31 years of age, married, one child, residing in Costa Rica, was assistant physician at 250 bed tuberculosis institution, wishes position in sanatorium in the United States where there is opportunity to learn chest surgery. Member, American College of Chest Physicians. For further information please address Box 227A, American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois.

Fellow, American College of Chest Physicians, chest surgeon, bronchoscopist, well trained, formerly member of university teaching staff, desires position in sanatorium. For further information please write Box 228A, American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois.

### MEDICAL SERVICE BUREAU

In accordance with a resolution adopted by the Board of Regents of the College at their annual meeting held in Chicago on June 17, 1945, a Medical Service Bureau has been established at the Executive Offices of the College for the purpose of serving the members of the College being released from the armed forces.

The Bureau would appreciate receiving information from the medical superintendents of sanatoria regarding positions available at their institutions, together with full particulars as to the type of position and salary offered. Fellows of the College who are looking for assistants should send complete information to the Bureau.

Physicians being released from the armed forces who are seeking appointments and positions should send complete information to the Bureau regarding their training and the type of position desired.

Please direct all correspondence to the Medical Service Bureau, American College of Chest Physicians, 500 North Dearborn Street, Chicago 10, Illinois.